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ORIGINAL ARTICLES

CURRENT TRENDS IN HEMATOLOGY

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INTRODUCTION

IT IS a great honor to have been chosen for the first Mead Johnson Award of 1948. As I look over the list of the distinguished men and women who were the earlier recipients of this Award I am aware of the obligation imposed upon me by your choice. At the same time I am grateful for the encouragement which this recognition will mean to my associates and to myself in our future work.

It goes without saying that the contributions which form the basis of your selection were the result of the work and the ideas of many members of our group at the Children's Hospital of Michigan. I want to pay special tribute to the memory of the late Dr. Thomas B. Cooley who founded the hematologic tradition in Detroit and who opened my eyes to the many interesting problems in this field.

A review of our studies on megaloblastic anemia of infancy was only recently presented to members of the Academy. To avoid repetition, I shall not summarize this work again in detail but merely take certain aspects of it as a pretext and point of departure for a larger and more pretentious subject which I propose to call current trends in hematology. In order to illustrate this theme, I shall draw freely on the work of others.

It is my belief that this topic is a timely one. In the last decade new tools of hematologic investigation have become available with the result that many basic concepts are even today undergoing profound modification. Because of the rapidity of these developments the newer concepts have not yet been generally applied in the clinical practice of pediatrics. They must be tested at the bedside and it may be expected that they will soon affect clinical thinking and action.

No longer is the hematologic scene dominated by descriptive morphology and by static

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arguments about the nomenclature of blood cells. These problems have been largely solved or recognized as limited in their significance. New avenues of research have been opened and hematology today is concerned with the solution to questions which could barely be asked only a short time ago. The ground work is being laid at last for a physiology of blood formation and destruction which will have direct clinical applications in the recognition, prevention and therapy of anemia.

The cellular mechanisms concerned in the production of blood cells are being studied by direct examination of aspirated bone marrow[1] and by tissue cultures of marrow cells.[2] By the method of aspiration the partial functions of the marrow organ, consisting in the reproduction, maturation and release of cells into the blood stream, can be analyzed to a large extent.[3] Disturbances in these functions can often be directly visualized. The effect of various substances and stimuli on the marrow can be studied in the patient or in the intact animal. Our knowledge of leukemia, pernicious and megaloblastic anemia, agranulocytosis, to name only a few conditions, has been greatly increased by the use of bone marrow aspiration. From the diagnostic viewpoint this technic has already become an indispensable tool which often discloses the nature of disorders not evident from the examination of the blood alone.

Considerable progress is also being made in regard to the chemical and nutritional aspects of blood formation. A number of investigators are studying endocrine influences on hematopoiesis, in particular, the role played by the hypophysis and the adrenals.[4] Systematic studies of the dietary factors needed for blood formation are being conducted in the laboratories of Wintrobe,[5] Elvehjem,[6] Whipple,[7] Sebrell,[8] and others. The role of minerals, proteins, amino acids and vitamins is undergoing exploration and we can now look forward to the day when a complete list of nutritional requirements for hematopoiesis will be available.[9]

The progress in this field has been paralleled by the intensive clinical investigation of nutritional anemias in recent years.[10–14] The discovery[15] of chemically pure hematopoietic agents such as folic acid and vitamin B_{12}, a substance which appears to be the crystalline form of liver principle, have greatly accelerated this type of research.

The capacity for hemoglobin production has been elucidated by the monumental series of experiments on anemic dogs in Whipple's laboratory.[16] On the clinical side we can begin to think similarly in terms of the total circulating hemoglobin mass and its loss and rate of replacement since the determination of the blood volume is rapidly becoming a practical measurement even in young infants. Knowledge of this kind will be necessary to the understanding of common problems in pediatric hematology, such as the anemia of prematurity and the changes in the blood of the newborn which have eluded us to date.

Our concept of iron metabolism has changed considerably and our understanding of the genesis of hypochromic or iron deficiency anemia has increased as the result of chemical studies by European[17, 18] and American[19] investigators and the use of radioactive isotopes of iron by Hahn and Whipple,[20] and Moore[21] and others. The absorption, transportation, utilization and storage of iron can be tentatively outlined today.

Measurements of the serum iron, for example, have shown characteristic absorption curves in iron deficiency states. These curves can be contrasted with the behavior of the serum iron under the influence of infection as Wintrobe[22] and his associates have done in an attempt to clarify the nature of the anemia associated with infection. Studies of this type are of special interest to the pediatrician. The mechanism by which infection produces anemia offers a challenge to pediatric hematology, which is so often concerned with what used to be called nutritional-infectious anemia.

Some years ago a large scale investigation of the chemical composition of the erythrocyte was begun by our good neighbors of the Children's Fund of Michigan at Detroit.[23] Although this work was tragically interrupted by the death of Dr. Erickson, it had already produced valuable information especially with respect to variations in different types of anemias. Long ago Whipple[24] pointed to evidence of abnormalities in pigment metabolism in Mediterranean anemia. Recently doubt has again been expressed that this disease is primarily a hemolytic process and some of us are thinking of the disturbance in terms of an inborn error of metabolism interfering with the synthesis of hemoglobin or substances in the erythrocyte stroma. The answer may be provided by the discovery of Shemin and Rittenberg[25] that glycine labeled with heavy N is a precursor of the pyrrole ring in porphyrin, heme and its degradation products, the bile pigments. Heavy N glycine can thus be used to trace the synthesis, destruction and excretion of these substances. By following the labeled glycine molecules through the metabolism of patients with Mediterranean anemia, it may be possible to demonstrate a defect in pigment synthesis.

These are examples of present methods and problems relating to the formation of blood. Thanks to the studies of Watson,[26] Ponder[27] and Dameshek,[28] a great deal of progress has also been made in the study of mechanisms involved in blood destruction. I can mention only two of many recent advances in this field: The determination of the life span of erythrocytes by means of the differential agglutination of transfused red blood cells[29] enables us to study the survival of these cells under normal and pathologic conditions. The discovery of the Rh antigens by Landsteiner and Wiener,[30] the recognition of their role in erythroblastosis by Levine[31] and the development of technics for the determination of antibodies by Diamond,[32] Witebsky,[33] Coombs,[34] and others have revolutionized our concepts of erythroblastosis and stimulated immunologic research into other hemolytic anemias.

This sketchy outline indicates in a general way the tremendous expansion which is taking place in hematology and the extent to which thinking in this field is turning into physiologic channels. I should like to illustrate this point by a few small but specific problems with which I have had personal experience.

In our study of megaloblastic anemia, the original tool was a morphologic one and the task consisted in the recognition and definition of an abnormal pattern in the cytology and cellular composition of the bone marrow.[35] Once this was done the specific nature of these alterations could be tested by the use of biologic substances, liver and folic acid. The morphologic criteria could then be enlarged and refined and the true incidence of the condition could be determined. It thus became possible to explore the nature of the disturbance in marrow physiology and by serial and semiquantitative analysis of the marrow to show that a defect in mitotic reproduction of blood cell precursors was present.[36] From the effect of therapeutic trials it seemed reasonable to infer the presence of a deficiency. Analysis of clinical data seemed to implicate infection and dietary intake as possible factors in the genesis of such a deficiency.[37] From this point on the problem became largely a nutritional one and required new tools, chemical and bio-assay methods to determine the nature of the deficiency and experimental production of a comparable anemia in animals on diets deficient in the factors suspected. The studies of Elvehjem, of Bethell[38] in Ann Arbor and those now being conducted by May and his associates[39] in Minneapolis are of this type and the center of interest has shifted to their work. This rapid development of a problem from a morphologic observation through clinical analysis and physiologic correlation to a purely nutritional study exemplifies the range of methods and the scope of hematology today.

The point can be equally well illustrated by the history of erythroblastosis fetalis. The work of Diamond and his associates[40] established the essential unity of the three main variants of the disease on the basis of clinical and morphologic observations and laid the foundation for the study of the hematology and pathology of erythroblastosis. With the discovery of the role played by Rh antigens and antibodies the problem suddenly shifted into the field of immunology. As the new tools and investigation became available, the concept of the disease changed radically. Erythroblastosis fetalis became hemolytic disease of the newborn.[41]

For a moment it seemed as if the problem were solved. Maternal antibodies of varying concentration and quality reacting with fetal antigen present exclusively in the erythrocytes caused a hemolytic anemia which in turn was thought to account for all the other manifestations of the disease. Yet it seems clear today that some of the simplified and confident assumptions embodied in the first immunologic theories of erythroblastosis will not stand the test of clinical observation, at least not in their original form. There has been surprisingly little correlation between the behavior in vitro of maternal antibodies and the manifestations of the disease in the infant. In our own experience high titers of antibodies have frequently been associated with mild clinical disturbances and vice versa. We have not as yet been able to demonstrate a correlation between the type of maternal antibody and the type of fetal disease.[42] We may conclude that the mode of action of the antibodies on the fetus remains at present obscure. Studies of British authors[43] and of Witebsky[44] in this country suggest the presence of Rh antigen in tissue cells. Observations on the pathology of erythroblastosis seem to us in keeping with the possibility of a direct antigen-antibody reaction taking place in various organs. On the basis of these studies it seems likely that hemolytic anemia does not in itself account for the pathology or the disturbance in physiology associated with erythroblastosis fetalis but is only one of the manifestations of a far more general effect of the disease on the fetal body.

The need for a broader concept of the pathogenesis of the disease is also evident from the failure of the current theories of erythroblastosis to account for one of its most interesting manifestations, kernicterus. Studies now in progress in our laboratory indicate that this phenomenon is not even specific for erythroblastosis. A comparison of 22 autopsy cases of kernicterus in infants with proved erythroblastosis with 25 other similarly studied cases in which erythroblastosis fetalis was not present revealed the same distribution of pigment in the brain and the same histopathologic changes; yet in most other respects the two groups were dissimilar. Prematurity and infection rather than hemolytic processes seemed to be the predisposing if not etiologic factors in the second group. If these findings are confirmed, a comprehensive theory of kernicterus must include them and explain the disorder in terms of neurophysiologic mechanisms of the newborn which the immunologic concept in its present limited form does not provide.

Another thought-provoking aspect of erythroblastosis has been all but forgotten in the general preoccupation with immunologic problems. I refer to the phenomena of extramedullary hemopoiesis and erythroblastemia. The meaning of these findings remains obscure. It is interesting to recall that in their first publication on the subject Diamond and his associates[40] pointed out that extramedullary hemopoiesis cannot be correlated with the presence or degree of anemia and therefore cannot be regarded as a compensatory mechanism. This has since been borne out by the studies of Miller[45] at New Haven who showed the striking similarity in the pathology of erythroblastosis and of infants of diabetic mothers. In the latter group marked extramedullary hemopoiesis occurs in the

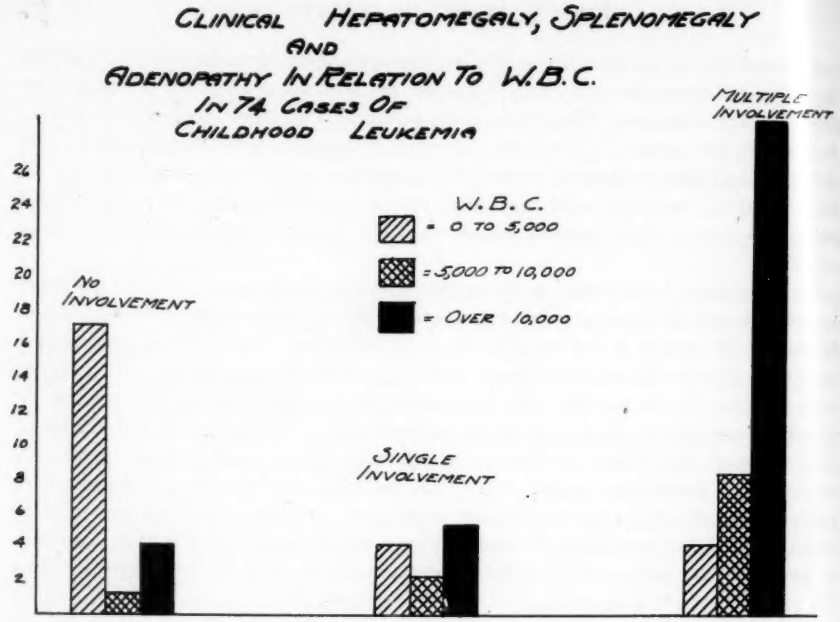
complete absence of anemia. Extramedullary hemopoiesis has been shown to be a common finding in toxoplasmosis and it is well known that it occurs in a number of other, sometimes obscure, conditions. What, then, is the significance of extramedullary hemopoiesis? Is it simply the response of the fetal and infantile organism to prolonged hypoxia from any cause and thus comparable to marrow hyperplasia under similar conditions in later life? Pathology and experimental pathology may well provide the answer to this problem which has clinical and diagnostic significance, as I hope to indicate in my concluding remarks.

Extramedullary hemopoiesis in the spleen, liver and other organs provides a possible source of blood cells and therefore has a bearing on the interpretation of blood pictures. Normally the marrow is the only site of blood formation. Under normal conditions at least only mature cells enter the blood stream, or, expressed in a different way, immature cells cannot leave the marrow. The Swiss hematologist, Rohr,[3] has pointed out that the marrow spaces seem to form a closed system which does not communicate with the blood. The release of cells into the circulation would therefore seem to require special mechanisms related to the maturation of cells. In contrast the open circulation of such organs as the spleen offers no special problem to the entrance of cells into the blood stream. Rohr suggested that the appearance of immature cells in the blood indicates their formation at extramedullary sites rather than their premature release from the bone marrow. Many observations seem to support this theory. Immature cells abound in fetal blood during the period of hepatic hempoiesis and disappear when blood formation becomes limited to the marrow. A comparison of blood findings and tissue changes in erythroblastosis shows excellent correlation between the extent of extramedullary hemopoiesis and the number of immature cells in the blood. The same is true in regard to Mediterranean anemia and many other conditions.

It would seem that this relationship between extramedullary hemopoiesis and the presence of immature cells in the blood applies also to leukemia. The limitation of the leukemic process to the marrow would result in leukopenia if the immature cells were unable to leave the marrow, since mature leukocytes are produced only in small numbers. With involvement of lymph nodes, spleen, liver or other organs the pathologic cells produced at these sites may enter the blood and the typical leukemic blood picture may result. This theory explains the paradox that the marrow as a rule shows the same hyperplastic immature pattern whether the blood picture is leukemic or aleukemic.

An analysis of 75 cases of leukemia which is now being completed in our laboratory shows rather good correlation between clinical evidence of organ involvement outside the marrow on the one hand and the presence or absence of leukocytosis on the other (Fig. 1), supporting the idea that the pathologic leukocytes in leukemic blood indicate extension of the disease beyond the marrow. These observations appear significant because they also seem to correlate with the duration of the leukemic process, and with the occurrence of remissions.

The graph in Figure 2 shows that of the patients with acute stem cell leukemia whose blood picture showed leukopenia many survived beyond four months after the onset of symptoms, whereas none of the children with high white blood counts lived for that length of time and most of them died much sooner, usually within two months. Likewise, the occurrence of spontaneous remissions was virtually limited to the group with leukopenia. In this group the incidence of spontaneous remissions was 33%, as compared with an incidence of only 5% in patients with hyperleukocytosis and 18% in the entire group of acute stem cell leukemias.


CLINICAL HEPATOMEGALY, SPLENOMEGALY
AND
ADENOPATHY IN RELATION TO W.B.C.
IN 74 CASES OF
CHILDHOOD LEUKEMIA
MULTIPLE INVOLVEMENT
W.B.C.
= 0 TO 5,000
= 5,000 TO 10,000
= OVER 10,000
NO INVOLVEMENT
SINGLE INVOLVEMENT
26
24
22
20
18
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8
6
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2

FIG. 1

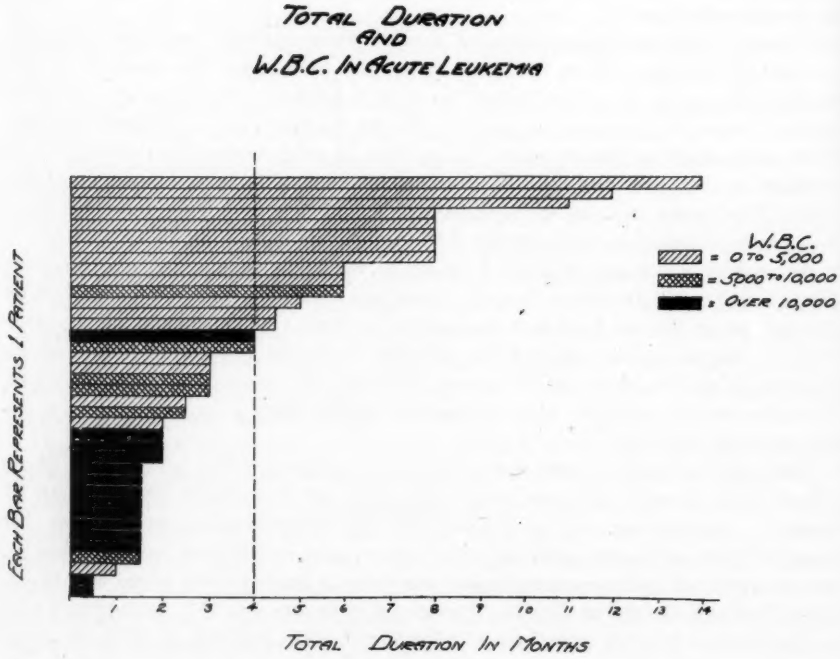
TOTAL DURATION
AND
W.B.C. IN ACUTE LEUKEMIA
W.B.C.
= 0 TO 5,000
= 5,000 TO 10,000
= OVER 10,000
EACH BAR REPRESENTS 1 PATIENT
1
2
3
4
5
6
7
8
9
10
11
12
13
14
TOTAL DURATION IN MONTHS

FIG. 2

The work of Dr. Farber and his associates[46] on remissions in leukemia induced by folic acid antagonists, which will be presented later at this meeting, makes these observations more significant than they otherwise would have been. They seem to us to indicate that the natural course of the disease has a significant relation to the white blood count which in turn seems to depend on involvement of extramedullary organs. Our evidence, which will be presented in detail elsewhere, suggests that duration is prolonged and spontaneous remission possible in patients in whom the leukemic process is for a time at least limited to the marrow. Conversely in patients where high leukocyte count indicates early involvement of other organs the course is short and remissions are unlikely. Perhaps these hemopathologic observations, which need to be confirmed, will provide a clue to the relation of leukemia to cancer in general.

In this presentation I have tried to illustrate the fact that hematology has been revitalized and correlated with a wide range of clinical and physiologic problems. The examples I have chosen mainly with reference to the subject of anemia could be duplicated in every branch of hematology. Today hematology is no longer an isolated field of endeavor but serves and utilizes at the same time many and widely divergent disciplines such as nutrition, chemistry, immunology, cellular physiology, pathology, genetics and, above all, clinical medicine. I should like to think that my remarks will contribute in a small way to the task of maintaining the unity of the clinical and the investigative viewpoint.

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CLINICAL CONCEPT OF POLIOMYELITIS

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EVERY aspect of poliomyelitis has been subjected to intensive study during the last two or three decades, in spite of which the clinician has not been presented with any inescapably sound doctrine regarding its epidemiology and transmission, its precise pathogenesis, or the details of diagnosis and treatment. The clinician, who observes the only animal naturally subject to this disease, must develop his own credo regarding most of the aspects of the human form of the disease including not only the details of management of the affected patient but also the many hypothetic considerations which influence one's judgment during epidemics.

This paper is an effort to summarize our own ideas during the observation of more than 1000 cases. We hope later to document certain of our clinical impressions by detailed analysis of this case material. At present, however, we are attempting simply to record the point of view with which we have approached the many inscrutable aspects of this disease. As long as this disease continues unpredictable in course, severity and end result and cannot be made to reproduce in animals the counterpart of epidemic disease in man, purely clinical considerations must have some weight. Reasoning which may be largely inductive may point the way to useful hypotheses.

EPIDEMIOLOGY

The epidemiology of the disease remains obscure. There has been a tendency to depart from an early theory that the disease spreads by means of direct contact. The abundant occurrence of the virus in the intestinal tract of affected patients has led to the belief that the manner of spread resembled that of the enteric infections. Our more recent cases have presented so many instances in which contact infection seems to be the likely method of transmission as to indicate that this is at least one important epidemiologic mechanism.

There is undoubted significance in the recent observations that the virus may be present in the feces of patients to such an extent that it may be recovered from the sewage in an epidemic area. This provides a method for widespread dissemination amongst a population in which filth, flies and direct contact contribute to the contamination of food, drink and fomites.

Opportunities for the distribution of fecal infection are multitudinous. It is most plausible that if the virus of poliomyelitis is transmitted by way of fecal soilage opportunities for infection are far more common than evidences of clinical disease.

Numerous observers have suggested that primitive and unsanitary living conditions offer an opportunity for infection in infancy as a common occurrence and that at this age period paralytic symptoms appear infrequently thus raising the general level of

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immunity in the population by virtue of silent infections. This theory attempts to account for the probable fact that better sanitation and a more protected environment seems to be accompanied by an increase in the paralytic form of the disease in older age groups.

Subclinical Infection

Clinical disease may not be immediately dependent upon exposure. The virus has been isolated from stools of the patient before there was evident disease, during and after evidences of infection, and from those who lacked any evidence of infection. Antibodies have similarly been detected in the blood of those who seemed to be perfectly healthy previously. These findings are commonly advanced as evidences of the frequency of mild subclinical attacks of poliomyelitis.

In contrast to such a theory there is a possibility that such an extremely ubiquitous virus may achieve complete latency in many healthy persons: a state of perfect parasitism in which the organism may be maintained within the nerve cell (the only medium in which the virus has been shown to perpetuate itself) without the necessity for any destructive or inflammatory cellular response. In such a state of latent infection, neither the demonstrable presence of virus nor the presence of immune bodies in the blood need constitute irrefutable proof of disease in the sense of an inflammatory response. The development of pathologic change in the nerve cells might then be entirely lacking or might await adventitious factors affecting host susceptibility. It may, in this disease, be less important to study the seed and how it is sown than to investigate the soil, the factors which permit opportunities for infection to eventuate in recognizable disease.

We recognize the refractoriness of most experimental animals against infection and the necessity for the use of highly artificial methods of inoculation for some other animals but, apart from the putative protective effect of specific immune substances, we have little regarded factors which determine human susceptibility.

There are many examples in which a parasite lives within a host without any disturbance to either host or parasite until this relationship is interfered with by some adventitious factor. 1. The colon bacillus constantly inhabits the human intestine and produces disease only when some injury to the bowel or urinary tract occurs. 2. Herpes simplex virus may remain latent in the nervous system for years to produce symptoms only in the presence of unrelated disease or injury. 3. Animals which are inoculated intracerebrally for the production of experimental virus infections frequently develop disease which is subsequently shown to be due to a virus latent in the experimental animal and not to the inoculum. One may multiply the examples of various pathogens which may live and multiply within a living host for varying periods of time and which produce disease only upon the introduction of some provoking factor. It may be difficult to apply a similar concept to the pathogenesis of poliomyelitis but this may none the less be true.

How else is one to explain the importance of many well known precipitating factors? Innumerable observations point to the importance of injury, chilling, fatigue, tonsillectomy, pregnancy, etc., in provoking symptoms of this disease. It is difficult to assume that such factors operate to introduce the virus and often this possibility is belied by the immediacy with which such symptoms follow these incidents. It is unlikely that these precipitating causes happen simply to coincide with advancing inflammatory change in the nerve cells. An attractive hypothesis is that these provoking causes convert latent benign infection of the nervous tissue (or elsewhere?) into progressive inflammatory disease.

Biphasic Febrile Course

Nor are these possible factors which may convert latent infection into active disease limited to purely physical trauma. The biphasic temperature curve of poliomyelitis is frequently and faithfully recorded. Some accounts regard this as occurring in from 20% to 35% of cases. It is significant that this biphasic temperature course is more a matter of the patient's history than of direct clinical observation. The recent comment of the Minnesota study[1] describes 22% of their cases in this category although "none of these patients who were hospitalized early showed the phenomenon of recurrence of symptoms." It has not been definitely proved that the first stage of temperature rise in the biphasic febrile pattern is due to an inflammatory response to the specific virus. The experimental evidence supports the view that the virus infects only nerve cells. It is accordingly difficult to support a theory that a febrile rise which precedes the usual preparalytic fever is due to systemic invasion prior to and apart from the invasion of the nervous system. The symptoms described in the initial phase are vague and variable, little resemble the so-called second phase and include such manifestations as sore throat and upper respiratory symptoms of which poliomyelitic virus seems an unlikely incitant. We have no good example in the series of cases which we have observed in the hospital of a truly biphasic course of the disease. We do have a number of instances, perhaps insufficient to prove a possible thesis, in which prior infection with an unrelated pathogen accompanied by objective findings and fever: tonsillitis, pneumonia, scarlet fever and numerous upper respiratory infections, preceded by a few days the onset of classical early symptoms of poliomyelitis.

Bacterial Traumatic Factors

Our observations cause us to believe that a variety of viral and bacterial agents may be responsible for infections which precede poliomyelitis and which serve as traumatic factors of exactly the same order as tonsillectomy and other predisposing causes of generally admitted significance.

It does not help much to supplant the term "dromedary" with "bactrian poliomyelitis" except perhaps to clarify the number of humps in these particular members of the camel family. There is plenty of room for doubt that a biphasic course characterizes any significant proportion of the cases of poliomyelitis. Our own experience supports the view that the essential course of poliomyelitis consists of a single period of elevated fever.

Clinical Considerations—Early Symptoms and Signs

In the consideration of the actual case there are a few conclusions which might be listed without the assurance that these will meet with general agreement. First among these concerns the early symptomatology. This is meager and is frequently overstated. Fever, headache, malaise are usually present and together with other evidences of mild illness completely fail to differentiate the disease from many common infections. Conspicuously lacking, in the preparalytic period, are the frequently expected evidences of increased intracranial pressure and of marked meningeal irritation.

Examination at an early stage nearly always reveals only slight neck stiffness which is elicited in only the last few degrees of flexion. Weakness, except that involving the cranial nerve supply—and cranial nerve paresis may appear very early—is a later development. Marked stiffness of the neck, back and hamstring accompanies the later stage of

the disease. The late accession of this typical stiffness is of considerable value in differentiation of poliomyelitis from many of the other central nervous system diseases in which, as improvement occurs in the active course of infection, there is corresponding and coincident regression of the signs of meningeal irritation.

Tremulousness of the musculature is a fairly frequent early sign and its localization may indicate the site of subsequent weakness.

Spinal Fluid Findings

The early and preparalytic diagnosis accordingly depends upon somewhat tenuous clinical evidence to which the spinal fluid examination is a valuable addition. The spinal fluid usually shows only an increased cell count and a moderate and somewhat progressive increase in the protein content. The spinal fluid pressure is not increased. The chemical findings apart from the protein are entirely normal. Even the cell count is occasionally normal, some observers state in as many as 50% of cases, but if only those patients are included in whom the diagnosis can otherwise indisputably be established, normal cytology will constitute only a small percentage. No conclusions can be drawn from the height of the cell count or the distribution of monocytes or polymorphonuclear cells regarding the stage or severity of the disease.

Sequelae

The sequelae of the febrile stage include muscle weakness, muscle spasm, pain, tenderness and hyperesthesia, muscle atrophy and vasomotor changes. It is reasonable to suppose that these factors are intimately interrelated but clinically this seems not to be invariably true.

Weakness is segmental and usually irregular and capricious in distribution. Consistently bilaterally symmetric weakness is a finding which is somewhat against the diagnosis. There is a decided tendency for improvement from the height of weakness but this is variable and unpredictable. Weakness may be obscured by pain and muscle spasm and may not be demonstrable in the recumbent position while the patient is still confined to bed. It is common practice to dismiss a fair proportion of patients at the end of the quarantine period as nonparalytic or abortive cases. In our experience, however, an extremely small number of those in whom the diagnosis is unquestionably established completely escape weakness. Weakness may be transitory and is frequently only mild, but none the less may carry the threat of later disability or deformity.

Many "abortive" patients will be found who cannot lift the head from the pillow, who cannot sit erect from the recumbent position with folded arms, who cannot execute a full squat from the standing position and rise unassisted. Moderate fatigue usually accentuates weakness and pronounced and continued fatigue may greatly increase residual weakness. It is extremely important to recognize minimal paresis and the accompanying demand for extended convalescence, continued observation and remedial care in the prevention of late deformity and significant residual weakness.

Muscle spasm, emphasized by the Kenny cult, reaches its height somewhat later than does muscle weakness. Almost certainly there is no constant reciprocal relationship between weakness and spasm. In contrast to weakness, muscle spasm is far more symmetric in its distribution. The physiology of muscle spasm is poorly understood but through muscle shortening and succeeding fibrosis it may produce disability and significant deformity. Persistent muscle spasm requires the same careful after-care as does muscle weakness.

Tenderness, hyperesthesia, pain, atrophy and vasomotor changes irregularly accompany weakness and must be included in any complete concept of therapy.

The search for a specific therapeutic agent has not been fruitful and there are those who believe that search for such an agent is foredoomed to failure because the virus exists only within nerve cells where it is relatively inaccessible to therapy and because early symptoms derive from advanced cellular damage.

The evaluation of therapy with any chosen agent is beset with the difficulty of selecting an adequate end point as the basis of comparison of treated and untreated cases. The clinical course is so variable and so unpredictable that it is almost impossible to conduct a controlled experiment which will provide a significant answer to this problem. The outcome presents a spectrum with imperceptible gradations between the nonparalytic case and the one which shows severe paralysis. Arbitrary division into paralytic and nonparalytic categories is fictitious if mild or transitory weakness is disregarded. The presence or absence of paralysis depends on objective analysis which will vary with the observer. Only an agent of extreme potency can displace the spectrum of outcome unmistakably in the direction of nonparalytic end results and the introduction of even such an agent may have long to wait for complete acceptance.

Perhaps to some readers it will weaken the argument of this paper to state a belief that human blood, convalescent serum or normal plasma beneficially affect the course of this disease if given early. Such preparations are unquestionably weak therapeutic agents but they seem to us to favor, even if they do not promise, an improved end result. The theory upon which such agents were initially employed depends upon the presence of antiviral agents in the blood of convalescents and of normal persons. Assuredly these immune bodies are present in only small amounts of an order which would not lead one to expect therapeutic effectiveness to any great degree. The response of viral infections to serum immune substances is notoriously unreliable. Curious beneficial results are sometimes seen, however, in measles following the administration of convalescent serum at an advanced stage of infection and we have seen an inadvertent therapeutic effect in varicella when transfusions were given for another purpose in the course of active infection. Conceivably the patient may be benefited by an effect which is not comparable to that secured by serums of high potency or to the antibiotic and chemotherapeutic agents in use in other infections.

The admittedly meager effects from the administration of human blood preparations may not depend upon antibody action at all but may depend upon substances apart from specific antibodies which are inimical to the advance of infection. If adequate precautions are observed there is little prospect of harm from these preparations and the beneficial effects may be comparable to the supportive value of blood and blood products in the treatment of other serious unrelated infections.

It may be justifiable to speculate at this point upon the possible effectiveness of a specific method of immunization against this infection. The immune response against a minute antigen, of which poliomyelitis virus is the perfect example, is generally poor. Patients have been known to contract poliomyelitis after they have been shown to possess demonstrable amounts of serum immune substances. When one considers the usual incidence of poliomyelitis among a population it would appear to be a task of incalculable magnitude to demonstrate that the production of immune substances by any method of active immunization will be followed by resistance to clinical infection. Solution of this approach for prevention would necessitate a mass experiment in which success

could only be attained by promising much more in advance than would be justified by the probabilities.

It seems far more likely that an eventual solution to the therapy of poliomyelitis will lie in the development of a therapeutic aid which, like certain well known analogies, might interfere with the essential enzyme system of the virus upon which the life cycle of such an intracellular parasite depends.

Treatment of the Paralytic Stage

The early treatment of the paralytic stage is entirely symptomatic. It is a manifest absurdity to expect that therapy directed toward the affected musculature can modify the underlying damage to the nervous system. Early measures are suited only to maximum comfort of the patient and are accomplished by careful nursing, gentle handling, enforced recumbency and protection of the musculature against painful stimuli, fatigue and over-stretching. It is possible to determine the status of the patient with the avoidance of pain and fatigue. As a matter of fact, examination of the patient during the acute and painful stage should be infrequent, should not distress the patient and need only detect such weakness and other signs as demand immediate active treatment. Early complete muscle tests cause unwarranted pain and fatigue to no good purpose. Painful symptoms are often best treated by the application of heat. Many patients gratefully accept the hot wool packs but other forms of heat may equally well be employed with due regard to the comfort thus afforded. Early institution of heat treatment does help to relieve pain, encourages the circulation and the nutrition of affected musculature and seems to minimize vascular complications such as thrombophlebitis. Certainly there needs to be no fetish regarding the use of heat in the early stage for the benefit thus secured is completely reflected in the state of comfort of the patient and any result secured in the final state of the patient is to be expected only from the relief of pain and tenderness during the acute stage.

Restoration of function in muscles affected either by spasm or by weakness is best served by measures which preserve normal muscle length through the prevention of shortening or of over-stretching. The extremities may be supported in physiologic position by means of various devices including special beds, sand bags and braces. It is important that rigid immobilization, which interferes with circulation and impairs nutrition, be sedulously avoided. There is no reason, however, why the use of many devices to maintain the trunk and extremities in a good position of rest and comfort should be abandoned because of the perfectly cogent warnings against rigid immobilization by casts and braces.

With the subsidence of fever and the gradual loss of extreme tenderness, passive motion of the musculature may be carefully carried out with the movement of each joint through its entire range of motion in order to maintain normal joint function and to promote the maintenance of normal muscle length. Early institution of passive motion, within the limitations imposed by tenderness and pain, serves importantly to minimize muscle shortening and succeeding fibrosis and furthers the eventual restoration of more useful function. Passive exercises should not be limited to the extremities but, so far as possible, should include the spine and the entire body.

Drugs have been employed for the relief of muscle spasm. Neostigmine has had some acceptance[2] for this purpose although in our hands results have been equivocal—with an occasional case in which there seemed to be some good effect. Curare has been advocated with an enthusiasm[3] which seems not to have been generally shared.

Special Considerations

Many problems arise in the course of this disease which may not be considered here in great detail. Respiratory failure of spinal origin frequently accompanies shoulder girdle weakness. This should be watched for if one deltoid is involved and should be expected if both deltoids are weakened.[4] The intercostal muscles are most frequently involved although the diaphragm may similarly be weakened with the production of somewhat different symptomatology. The respirator is of inestimable value if it is skillfully employed for adequate reason. The patient who has reached the stage of severe respiratory difficulty will secure great relief by the use of this machine although the patient with less respiratory embarrassment may find the machine terrifyingly unpleasant and thus may complicate the necessity for its later use. It is important to study the patient to determine when the use of the machine is necessary and meanwhile to gain his confidence and to quiet his fears.

Respiratory failure of bulbar origin with involvement of the central mechanism of respiration has long been recognized as a much more difficult problem. These patients have irregular respirations accompanied by hiccough and by voluntary efforts which make it difficult to secure successful adaptation to the assistance of the respirator. In many of these patients there is coincidental circulatory failure and occasionally the phenomenon of severe pulmonary edema. Accompanying weakness of the muscles of the pharynx and larynx is sometimes so extreme that relaxation of the tissues obstructs respiration and coincidentally the patient may have an accumulation of saliva and mucus which he may be unable to swallow or to expectorate. In such cases, tracheotomy is sometimes advisable. The selection of cases in which this procedure should be employed requires great judgment and experience lest the patient simply be confronted with another problem instead of securing relief of his symptoms. Instrumental methods of determining anoxia are not generally available and clinicians of sufficient experience to determine that tracheotomy is necessary are even less generally available. There is present in severe bulbar poliomyelitis the dreadful urgency to do something. Tracheotomy should not be employed unless there is unmistakable evidence that progressive anoxia is dependent upon an obstruction of the airway which can be relieved by tracheotomy. Obstructions at a low level in the respiratory tract may necessitate bronchoscopy and may be completely unrelieved by tracheotomy.

It has long been recognized that cerebral anoxia may be a serious concomitant of respiratory weakness. Mild degrees may escape recognition and may be responsible for mental confusion and mistaken for encephalitic involvement.[5] Significant degrees of anoxia may exist before cyanosis is apparent. The prevention of anoxia involves, in addition to the respirator and tracheotomy, the administration of oxygen by mask, by intranasal catheter or through a tracheotomy opening, and oxygen therapy should often be employed long before anoxia is unmistakably apparent.

Weakness in swallowing, in which there is frequently concomitant respiratory weakness, may necessitate parenteral feeding. Gavage feeding should never be employed until there is considerable improvement in the patient lest there be aspiration of regurgitated food and fluids. A safer course is to allow the patient to subsist on a minimum of food and fluids given parenterally during the early stages of this form of disease. No ill effects result from moderate dehydration and starvation for a short time and excessive hydration should carefully be avoided. Meanwhile postural drainage, as originally suggested by Durand,[6] is highly important to prevent the accumulation of unswallowed fluid with the accompanying frequent use of suction in the pharynx.

The respirator patient or any one with similarly profound weakness imposes great responsibility upon his attendants for his total care. It is necessary to watch his comfort, to carry out with suitable restraint all of the general therapeutic measures and to enforce adequate nursing care, especially in the prevention of decubitus ulceration. A maximum of skilled teamwork must be provided.

Impaired function of the bladder and bowel are frequently a problem. Sphincter difficulties frequently result in failure to void and distention of the urinary bladder during the early course. Repeated catheterization is usually indicated for this complication and normal emptying of the bladder commonly returns within a week after onset. In more obstinate cases, tidal drainage is sometimes advisable. Certain drugs such as furmethide[7] have been used with some success to promote bladder emptying; we have used them rarely and with great misgiving. Sulfonamides are frequently used as urinary antiseptics when repeated catheterization is necessary, although in our experience this seems to result only in equally severe infections with sulfonamide-resistant organisms. It may be preferable usually to treat urinary infection only after normal urination has been established when the colon bacillus, which readily yields to therapy, is the usual pathogen.

Constipation is the rule in early poliomyelitis and is difficult to combat. Cathartics are generally ineffective. Enemas are necessary to keep the lower bowel clear, otherwise fecal impactions commonly occur. Bowel difficulties, unlike those of the urinary bladder, are frequently prolonged into convalescence. The presence of obstinate constipation may sometimes be utilized to good effect in the administration of fluids by rectum to the patient who cannot swallow.

Later Care

As the patient passes the peak of pain, weakness and muscle spasm, gentle manipulation must be earnestly continued to maintain flexibility of the joints and to promote and restore normal muscle length with the prevention of shortening and fibrous changes. Painstaking re-education of muscle function is in order that the patient may learn to use weakened members to his best advantage. This type of laborious re-education is one of the most significant advances in treatment in which the well trained and resourceful physical therapist has proved to be invaluable. The patient must learn to use his residual strength to the best possible advantage and to develop a pattern which utilizes weakened muscles to their optimum power in the task of serviceable locomotion and other forms of activity. This involves also the prevention of awkward and inefficient use of undamaged muscles as substitutes for paretic muscles. Even in some of those without marked weakness it will be necessary for the patient to relearn some of the complicated integration of muscle function. Some of the damaged muscles may have their strength redeveloped in a manner which resembles those used by the physical culture devotees. The extent to which severely damaged extremities may be restored to useful function in spite of the persistence of extreme weakness may be most gratifying if adequate and painstaking re-education is employed.

During the later part of convalescence the advisability of using braces, splints and corsets must be considered. In some circles the use of such supports has been completely decried. As in most other considerations, one's judgment in this respect cannot be a matter of rule but must be governed by individual considerations. Some patients, who are sufficiently free from muscle spasm and have sufficiently regained their strength to permit locomotion and other activities, may still develop deformities as a result of

activity except for the judicious use of some form of bracing. The study of poliomyelitis is the observation of the patient and his proper care entails the utilization of everything which benefits his progress without concession to orthodoxy or dogma. The patient with good lower extremity strength may accomplish ambulation much more quickly if his weakened trunk is adequately supported. One who has quadriceps weakness may undertake weight bearing much more safely with one or another type of leg brace. These examples multiply and there is no reason why faulty strength should not be artificially supplemented provided only that one does not interfere too early with the patient's re-education toward normal mobility.

Surgical correction of deformity was formerly attempted with zeal which was perhaps mistaken but the realization of this fact need not now lead to invariable postponement of surgical measures to an extremely late stage. The consideration of surgical procedures should be individualized. Some of them may appropriately be carried out long before the expiration of an arbitrary period of one or two years.

The best care of the late sequelae of poliomyelitis can only be secured by integration of the efforts of several specialized fields of medicine. Above all is the necessity that some one physician maintain the over-all direction of the patient. We have not spoken of the psychologic or psychiatric difficulties which afflict certain of these patients nor of the necessity of rehabilitation of education and of earning power later on. Patients at times require the care of pediatrician, internist, orthopedist, the specialist in physical therapy, and the occasional specialized services of the surgeon, the bronchoscopist, the obstetrician, the urologist, the psychiatrist, the occupational therapist. Any one of several of these may best serve to direct the patient through his acute phase and his prolonged convalescence. It is not possible, however, to break up this care into numerous fractions which are not suitably integrated into adequate total care.

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Spanish Abstract

Concepto Clinico de la Poliomielitis

Este estudio está basado sobre aproximadamente 1000 casos de poliomielitis. Los estudios clínicos conciernen el único animal espontaneamente afectado. La extensión epidémica, ya se deba al contacto, ya a la contaminación fecal, puede resultar en infección latente convertida en enfermedad inflamatoria por numerosos factores traumáticos precipitantes.

No hay prueba de que la subida inicial de la temperatura en el curso bifásico sea debida al virus de la poliomielitis, y pueda ser que se deba a otra infección que obra como una causa precipitante.

Las secuelas de debilidad, el espasmo muscular, el dolor, la atrofia muscular, los cambios vasomotores no están necesariamente interrelacionados y pueden ocurrir independientemente. La debilidad

de los músculos es segmentaria y no simétrica. Cierto grado de debilidad generalmente ocurre si la diagnosis se establece con certeza; a menudo esto se pasa por alto cuando el tronco está afectado. El espasmo muscular alcanza su punto culminante más tarde que la debilidad, es más simétrico y la tiesura que ataca tarde ayuda a diferenciar éste de otras causas de irritación meníngea.

El tratamiento es sintomático y está dirigido especialmente hacia la preservación del largo normal del músculo: soporte contra el demasiado estiramiento y el estiramiento suave contra la contractura. El calor en cualquier forma es útil para aliviar el dolor y el espasmo muscular. Complicaciones especiales requieren tratamiento cuidadosamente diseñado. Es de gran importancia que se evite la anoxia.

El tratamiento tardío continua la preservación del largo normal del músculo y la re-educación gradual de la función integrante del músculo. Todos los métodos de tratamiento, incluyendo el uso de bragueros y tablillas y la corrección quirúrgica de más tarde de las deformidades, deben de ser individualizados y adapatados a cada paciente en particular.

Un médico debe dirigir a cada paciente y usar las diferentes habilidades médicas necesarias para el cuidado total y para guiar el paciente en sus propios esfuerzos hacia su restablecimiento.

384 Post Street

BALANCE AND ELECTROCARDIOGRAPHIC STUDIES IN A CHILD WITH POTASSIUM DEFICIENCY

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INTEREST in the correlation of the level of serum potassium with certain clinical states was first aroused by the demonstration by Biemond and Daniels[1] in 1934 that low levels of this ion regularly accompanied the muscular paralysis of familial periodic paralysis. It should be pointed out that in familial periodic paralysis reduction of serum potassium seems to result from transfer of potassium from the extracellular space to the intracellular space rather than from loss of the ion from the body as has been demonstrated by Gammon et al.[2] and Danowski et al.[3] Brown et al.[4] described a group of patients with renal disease in whom potassium deficiency was produced by excessive loss of the ion in the urine. Holler[5] described the occurrence of the condition in a patient recovering from diabetic acidosis. A similar report was made by Nicholson and Branning.[6] The metabolic basis for potassium deficiency in diabetic patients with acidosis has been well described.[7, 8] Darrow[9] and Govan and Darrow[10] have stressed loss of potassium occurring in infants with diarrhea and were the first to use potassium as a part of parenteral and oral repair therapy.

It is the purpose of this report to describe an instance of potassium deficiency occurring in a small child in whom there was an opportunity to follow the course of recovery by electrocardiograms as well as by measurement of balances of nitrogen and electrolytes during repair therapy.

CASE HISTORY

Patient was a 4 yr. old male child with extrophy of the bladder. Pyelography showed bilateral hydroureters and pelves at 3½ yrs. of age. A history was obtained at this time of repeated episodes of fever, diarrhea and vomiting which were interpreted as effects of recurrent urinary tract infection. Transplantation of the ureters into the sigmoid was done at this time. At 4 yrs. of age, he was admitted to the hospital with a history of fever, vomiting and diarrhea for 1 wk. On admission, he was severely dehydrated and acidotic. Treatment with sulfonamides, penicillin and parenteral fluids was immediately started. On the 1st day he received by slow intravenous drip 1050 ml. of solution made up of normal saline solution 600 ml. and 10% glucose solution 450 ml. On the 2nd day he received saline solution 350 ml., 10% glucose solution 730 ml. and normal plasma 285 ml. No oral feeding was given during this 48 hr. period. Fever subsided and he appeared well hydrated.

Blood was taken for chemical examination on the 2nd hospital day. During the forenoon of the 3rd day, muscular weakness appeared and in the course of 3 hrs. progressed to an alarming degree, accompanied by shallow and slow respiration. Heart sounds were faint and the pulse rate was 140/min. A clinical diagnosis of potassium deficiency was made and was supported by the report from the laboratory of low potassium, 2.5 mEq/l., in the plasma taken on the previous day (Table I). Electrocardiogram showed a normal PR interval but a prolonged QT interval. QRS interval was the upper limit of normal. There was marked depression of the ST segment and the T waves were low and diphasic. Corresponding measurement of plasma K subsequently reported from the laboratory showed a further large reduction, to 0.75 mEq/l.

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TABLE I

BALANCE DATA

Period*	Intake					Output Stool Plus Urine					Balance 24 Hrs.			
	ml. Vol.	mEq/l. Na	mEq/l. K	mEq/l. Cl	gm./l. N	ml. Vol.	mEq/l. Na	mEq/l. K	mEq/l. Cl	gm./l. N	mEq Na	mEq K	mEq Cl	gm. N
5/3–5/4	1036	93.4	25.8	77.4	0	440	27.5	9.5	41.4	9.42	+83.8	+22.5	+62.0	−4.15
5/4–5/5	1960	19.4	30.5	13.6	0	530	48.3	13.2	58.0	5.85	+12.4	+52.8	− 4.1	−3.10
5/5–5/6	1360	20.1	30.7	20.5	3.05	690	45.7	10.9	40.7	4.56	− 4.2	+34.2	− 0.3	+1.0
5/6–5/7	1475	13.1	35.2	9.9	1.27	750	55.2	19.5	24.0	4.07	−22.1	+37.4	− 3.4	−1.18

* Periods run from 12 a.m. to 12 a.m. on dates indicated.

Patient was placed on a metabolism bed and combined fecal and urinary excretion collected in 24 hr. periods. Separation of stools and urine was not possible because of the ureterosigmoid transplantation. Hourly ECG were made for the first 8 hrs. and then 3 times daily for the rest of the study, which lasted 4 days. All oral and parenteral intake was carefully measured and aliquots of each portion were saved for subsequent analyses. During the 1st 24 hrs. of the metabolic period 1047 ml. of the potassium-containing solution described by Govan and Darrow[10] were given by slow intravenous drip. After 18 hrs. of intravenous therapy, orange juice was begun by mouth and was well tolerated. Subsequently broths and milk were fed and on the last day of the study a soft solid diet was given. By the end of the initial 4 hrs. of treatment, when 525 ml. (containing K 18 mEq.) of intravenous potassium solution had been given, there was complete return of muscular strength and respiratory function to normal.

Convalescence was rapid so that patient could be discharged 2 days after completion of the studies. When seen again after a 6 mo. period, he was well and rapidly gaining control of bowel function. No further episodes of illness or weakness had occurred.

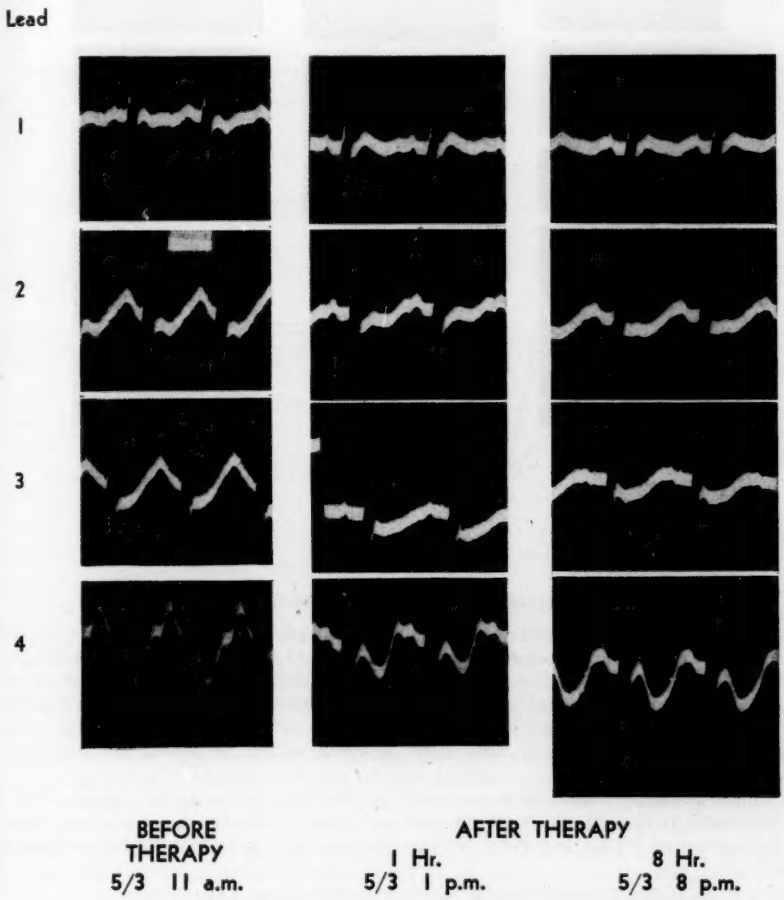

FIG. 1. Serial ECG taken at intervals following administration of K.

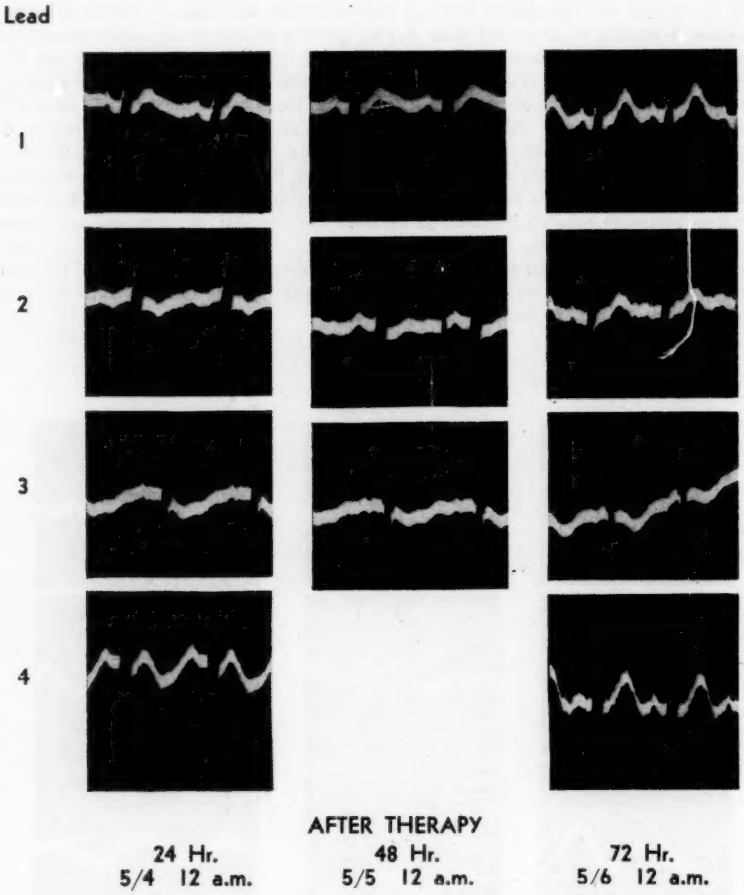

FIG. 1 (*Continued*)

EXPERIMENTAL PROCEDURE AND METHODS

Analysis of the intake was accomplished in the following fashion: All parenteral fluid was measured using a burette attached to the intravenous apparatus. All oral feedings were measured using a chemical graduate. After oral feeding was started, all intake offered was completely taken. On the 3rd and 4th day of the study, bread was added to the liquid diet. Analysis of the fluid part of the intake was done on aliquots of each type of feeding. Analysis of the bread intake was done using duplicate portions. Analytic data in Table I are presented without breakdown into component feedings.

Sodium and potassium analyses on serum excreta and diet were done using the internal standard flame photometer as described by Berry, Chappell and Barnes.[11] All chloride analyses were done using the method of Wilson and Ball.[12] Nitrogen analyses were done using the macro-Kjeldahl method.[13]

ELECTROCARDIOGRAPHIC AND SERUM POTASSIUM LEVEL CORRELATION

In Figure 1 are shown selected ECG taken ½ hr. before treatment, 1 hr. after, 8 hrs. after and on the 2nd, 3rd and 4th days of the study. At the end of the 1st hr., when only 125 ml. of the potassium

solution had been given, the ECG had returned almost to normal. However, the serum concentration of K measured 4 hrs. after the onset of treatment had risen to only 1.7 mEq./l. Potassium level rose to the slightly subnormal level of 3.8 mEq./l. on the 4th day of the study. The slow rise of serum K was accompanied by only minor changes in the ECG. Muscle strength, as judged by the child's ability to move and help himself, had returned to normal at the end of 6 to 8 hrs.

Balance Studies

Balance data found for Na, K, Cl and N are presented in Table I and graphically in Fig. 2.

Balance data describe a large retention of K, 82% of intake for the 4 day period. Presumably this represents replenishment of a large deficit. Using Darrow's[31] value of K 71 mEq./kg. body wt. a normal total body content for this patient would be 972 mEq. Retention measured over the 4 day period was 147 mEq. or 16% of expected body content. That this does not completely measure

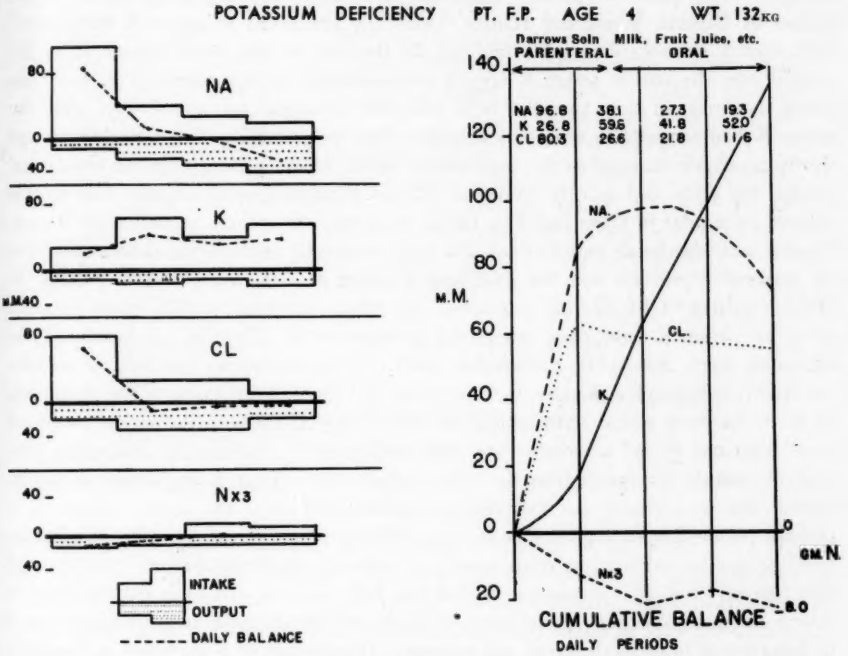

FIG. 2. Daily values for intake, output and balance are shown on left side of chart. On right side, balances are recorded additively. Figures at top of cumulative balance chart indicate amounts, in mEq, of intake producing charted balances. In order to observe deviation from normal relation of potassium and nitrogen balance, values for nitrogen in gm. x 3 are recorded on milliequivalent ordinate, normal intracellular ratio being K mEq.: N gm. = 3:1.

deficit at the outset of treatment is evident from the linear progress of retention across the 4 day period. Gamble, Wiese and Hansen[18] have recently described an instance of potassium deficiency in an infant with prolonged diarrhea. In their case, repair of the deficit, as judged by return of the serum potassium level and ECG to normal, was not accomplished until approximately 1/5 of the expected body content of K had been administered. Balance studies were not done in their case; however, applying the percentage retention found in our study to their data indicates an identical degree of retention to that found in the present case. In the absence of intake, nitrogen balance declines over the 1st 2 days. An ample intake on the 3rd day produced retention which a small intake on the 4th day did not sustain. The large progressive gain of K in the presence of a negative

nitrogen balance may be taken as evidence of an initial deficit which was much larger than the loss of N from the body. Sodium balance declines after a large initial gain on the 1st day. This might be due to reduction of intake after the 1st day but is much more probably due to the opposing effect of the large gains of K. Since an abundance of salt solution was given over the 2 days preceding the period of study, the initial deficit was presumably much larger than the sodium gain recorded in the chart.

Discussion

The lack of correlation between serum potassium levels and recovery of the ECG and muscular strength in patients with familial periodic paralysis has been noted by Gammon, Austin and Blithe[2] and Stewart, Smith and Milhorat.[16] In Holler's[5] patient, recovery had occurred before potassium balance could have been affected to any great degree. In the patient of Gamble, Wiese and Hansen,[15] similarly low levels of serum K were found with similar electrocardiographic findings. In the case of the latter authors, as in the present one, the rise in serum K lagged until relatively large amounts of K had been given; however, in their case the ECG remained abnormal for several days after the serum K had returned to normal. Presumably they were dealing with a prolonged and slowly reversible damage to the myocardium while in the present case the myocardial change was acute and quickly reversible. The electrocardiographic changes seen in this patient are similar to those found by the above mentioned authors as well as by Brown, Currens and Marchand[4] and Holler.[5] The most frequently encountered abnormalities are ST segment depression and low to absent T waves as seen in the present patient. In Holler's patient,[5] QRS slurring was noted. The effects noted in the ECG in the presence of a low serum K have been interpreted as evidence of defects in conduction of the excitation wave. Apparently the absolute level of K in the serum has little to do with the electrocardiographic changes. Evidence cited by Fenn[17] in his review of the physiology of K in the body would seem to indicate that relative changes in the serum potassium level from one period to another are more important in conditioning conduction phenomena than the divergence from the usual level of 4 to 5 mEq/l. It would seem as though neither the intracellular nor extracellular content of K was the critical factor. It is perhaps permissible to suggest that the astonishingly rapid therapeutic effect of administered K may be produced by concentration at cell surfaces during the process of passage into the cell fluid. It is reassuring to find that full repair of deficits is not necessary to relieve the acute situation. Rapid provision of K parenterally with accompanying hazard of harm to the heart is, therefore, not necessary. The quantity of K provided by Darrow's solution is apparently quite adequate.

The mechanism of the production of the potassium deficiency in this case seems fairly clear. In the week prior to admission, excessive vomiting of intake had occurred. Large losses of K must have occurred also in the stools. On the basis of low intake and excessive loss other factors arise tending to accentuate these deficits. Dehydration alone causes increased potassium loss.[18] After admission to the hospital large amounts of normal saline solution were given without any attempt to supply K. The administration of sodium chloride to man on a low potassium diet causes him to lose K.[19] With treatment with glucose and improvement of clinical condition, the formation of glycogen must have occurred; it is well known that this process requires K and that the blood K falls when glycogen is being stored.[20] The potassium content of the combined urinary-fecal excretion was so low in the face of a high intake that renal loss as a cause of the deficiency is not

possible. Because of the anatomic situation in this patient it was not possible to carry out renal function studies. A urine specimen obtained on the morning of the day when paralysis developed showed the low concentration of 6.5 mEq/l. This would seem to indicate that the kidney was capably conserving K.

Unfortunately, no initial body weight was obtained on this child and the last four Cl. analyses needed to complete Table II were lost in a laboratory accident. The omission of these data makes impossible the calculation of the shifts in body fluid compartments by the method outlined by Darrow.[9] However, the general trend of the sodium, potassium and chloride balances is in the direction that would be expected if Na had at first entered

TABLE II

BLOOD SERUM DATA

Date	Time	NPN mg./100 cc.	pHs	mEq/l. CO_2	mEq/l. Na	mEq/l. Cl	mEq/l. K
5/2	10 a.m.	52	7.27	18.0	144.0	110.0	2.5
5/3*	12 a.m.	—	—	—	148.0	109.0	0.75
5/3	4 p.m.	—	—	—	154.0	—	1.7
5/3	11 p.m.	—	—	—	151.0	—	1.8
5/4	10 a.m.	—	—	—	148.0	—	2.3
5/5	10 a.m.	40	—	—	143.0	—	3.0
5/6	10 a.m.	—	—	—	—	—	3.8

* Balance study begins at this point.

the cells and later been withdrawn as the potassium balance became positive.

Darrow et al.[21] have demonstrated that serum $NaHCo_3$ tends to vary directly with the intracellular Na and inversely with the muscle potassium content. Thus, when deficit of K exists and intracellular Na is high, the serum $NaHCO_3$ would be expected to be high. In the absence of more complete analyses of the serum for $NaHCO_3$ and Cl only an inference can be drawn as to the presence of such a distorted biologic equilibrium in the present patient. Examination of the serum sodium measurements in Table II reveals a rise in serum Na accompanying a sharp uptake of Na. In the patient of Gamble, Wiese and Hansen,[15] a similar rise in serum Na took place accompanied by a rise in serum $NaHCO_3$. It has been pointed out[21] that patients with potassium deficit may be expected to develop alkalosis when treated with Na and Cl. Darrow's solution is designed for the repair of both intracellular and extracellular deficits and contains considerably more Na than K, the concentration of the latter ion being limited by the amount that can be administered parenterally with safety. The cumulative curves of balance indicate that the large administration of Na on the first day hindered the retention of K. More efficient retention of K could probably have been obtained in this case if the parenterally administered ion had not been accompanied by Na.

Summary

An instance of potassium deficiency is described which was caused by excessive gastrointestinal loss, the parenteral administration of excessive NaCl and glucose and by lack of potassium intake.

The changes produced in the ECG are described.

Treatment with parenterally administered K was effective. Although a rise in the level of serum K accompanied the improvement, it returned to normal more slowly than the electrocardiogram and the clinical state.

The balances of Na, K, Cl and N during the recovery period are presented and discussed.

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SPANISH ABSTRACT

Estudios Electrocardiográficos y de Residuo en un Niño con Deficiencia de Potasio

A un niño de cuatro años con extrofia de la vejiga en quien se llevó a cabo una transplantación uretero-sigmoidea, le dieron severos vómitos, diarrea y fiebre. Fué tratado por deshidratación con glucosa y soluciones salinas intravenosamente. Al tercer día del tratamiento vino la debilidad muscular y respiratoria, se encontró que la sangre K era 0.75 mEq y ECG anormal. Los descubrimientos electrocardiográficos fueron intervalos QT prolongados, segmentos ST reducidos y ondas T difásicas bajas. Estos descubrimientos son diagnósticos de la deficiencia de potasio. La respuesta a la administración intravenosa de potasio fué dramática. La debilidad muscular desapareció dentro de una hora lo mismo que los cambios electrocardiográficos aunque la cantidad de suero potasio no regresó al estado normal por cuatro días. La medida del residuo K durante el período de cuatro días, en el cual se estudió el restablecimiento, demostró que K fué retenida al grado de 16% del contenido del cuerpo que se esperaba de este ion. Los datos indican que el restablecimiento de la función del músculo dañado había ocurrido mucho antes de que se alcanzara una porción significante de esta retención.

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RUPTURE OF THE SPLEEN IN AN ERYTHROBLASTOTIC INFANT

By EUGENE L. SLOTKOWSKI, M.D., AND ALBERT M. HAND, M.D.
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RUPTURE of the spleen in erythroblastotic infants is an unusual complication although many factors theoretically predispose to it. The shock-like state which may be present in erythroblastosis adds to the difficulty of making an antemortem diagnosis of a ruptured spleen.

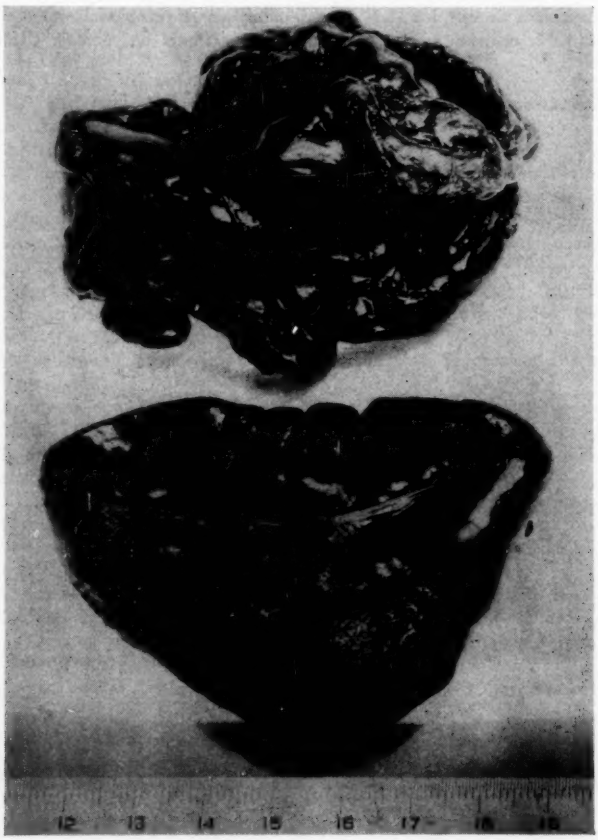

FIG. 1. Photograph of spleen (below) with tear in capsule. Extensive clot (above) shown for comparison.

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Case Report

Male infant M. was admitted to the hospital 16 hrs. after birth. At the time of delivery a yellow amniotic fluid and enlarged placenta were observed. The infant was jaundiced, lethargic and weighed 3.5 kg. Blood studies made approximately 12 hrs. after birth revealed Hgb. 4.5 gm./100 cc. blood, RBC 1.24 million/cmm. and 945 nucleated red cells/100 white cells in the peripheral blood smear. Mother was para III, gravida II, having delivered twins 2 yrs. previously. One twin died from "a knot in the umbilical cord"; the viable male twin became jaundiced the 2nd day of life but was not transfused. Both parents were Rh tested after the appearance of icterus in the viable twin and were

Fig. 2. Photomicrograph of hilus showing laceration and elevation of splenic capsule.

reported to be Rh positive. On admission to this hospital the patient was jaundiced, lethargic, and had generalized petechiae as large as 4 mm. in diameter. Temperature was 35.6° C. Respirations were depressed but the chest was clear on auscultation and heart tones were rapid and faint. Abdomen was rounded and tense and umbilical cord was dried but pulsating. Liver was felt at the level of the umbilicus and the spleen extended to the left iliac crest. Admitting impression was erythroblastosis, icterus gravis, and it was decided to carry out a replacement transfusion. Compatible group 0-Rh negative blood, 500 cc., was obtained from the Blood Center of the Michael Reese Research Foundation of Chicago. The blood infusion was started via a cutdown at 15 to 20 drops/min. and the left radial artery was dissected and exposed. Following the injection of heparin 0.2 cc. (200 u.) into the intravenous tubing, the radial artery was partially severed and blood escaped freely. At no time was the infusion of blood into the saphenous vein greater than 50 cc. ahead of the outflow from the radial artery. The infant did not manifest any respiratory difficulty and became more active during the 1st part of the procedure. Only 1 injection of heparin was administered. After 240 cc. blood had

been infused and 210 cc. removed, the infant suddenly became cyanotic and died in a matter of seconds. When the exsanguinated blood was discarded 3 hrs. later it had not coagulated.

Autopsy Findings: Externally, generalized petechiae and small ecchymotic areas, yellowish-orange discoloration to the skin and abdominal distention were noted. When the peritoneal cavity was opened, a large amount of fluid blood (50 to 75 cc.) ran out. Liver was enlarged, weighed 250 gm. (normal 78 gm.), and extended to the lateral aspect of the left abdominal wall. A 6 x 6 cm. clot was found in the left upper quadrant covering the under surface of the spleen and adjacent portions of the stomach, left kidney, transverse colon and the tail of the pancreas. Spleen weighed 42 gm. (normal

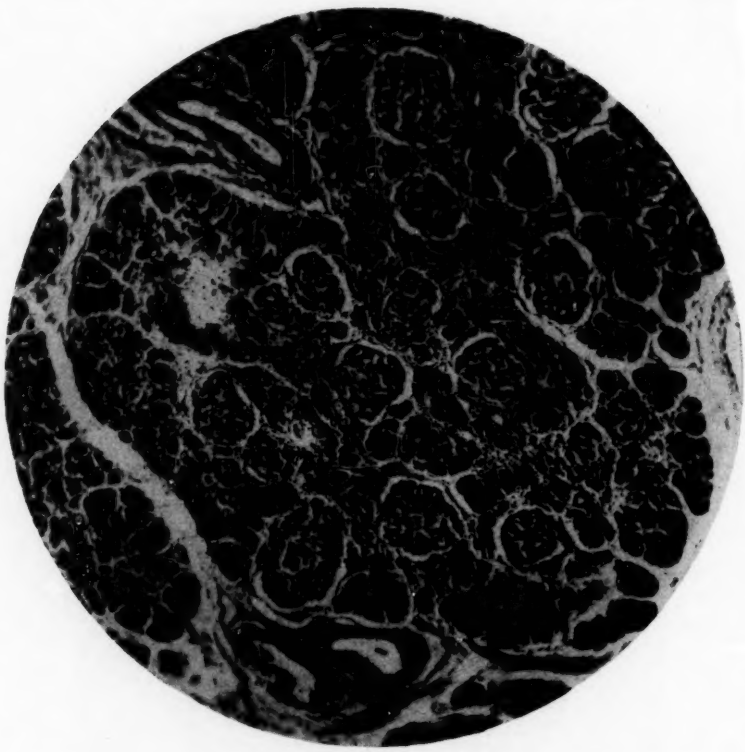

FIG. 3. Photomicrograph (×80) showing numerical and dimensional increase in pancreatic islets.

8 gm.) and the capsule was absent from the renal surface of the spleen in an area measuring 3 x 5 cm. in diameter (Fig. 1). The denuded surface appeared granular but there was no evidence of tearing into the parenchyma. Brain, thoracic and abdominal contents were covered with petechial hemorrhages.

Microscopically, the liver contained many foci of extramedullary hematopoiesis with large, localized masses of immature cells in the sinusoidal spaces. The splenic capsule and trabeculae were thinned, lymph follicles were markedly reduced in amount, germinal centers were absent and many immature red cells were present in the parenchyma. The capsule was elevated from the underlying parenchyma in sections from the hilus (Fig. 2). Islet tissue of the pancreas was increased numerically and dimensionally (Fig. 3). (Potter[1] mentions that enlargement of the islets has been noted in erythroblastotic infants but it is not common.)

Comment

A severe hemolytic process of the newborn was evidenced in this case by the early anemia, icterus, hepatosplenomegaly and high number of immature red cells in the peripheral blood. Heparin was used to facilitate removal of blood from the radial artery,

TABLE I

Typing of Family

Name	O-A-B	Rh°	Rh′	Rh″	Hr′	Classification
M-Wife	0	neg.	neg.	neg.	pos.	O-rh, Hr′ positive
M-Father	0	pos.	pos.	pos.	pos.	O-Rh1Rh2, H′ positive
P-Twin son, born 1946	0	pos.	neg.	pos.	pos.	O-Rh2, Hr′ positive
Twin son, born 1946	Dead—Knot in umbilical cord					
Baby M, born March 12, '48	0	pos.	Dead, icterus gravis			
Wife's mother	0	pos.	neg.	pos.	pos.	O-Rh2, Hr′ positive

Maternal Serum:
March 12, 1948: Positive for blocking antibodies, titer 32. No saline antibodies.
April 20, 1948: Positive for blocking antibodies, titer 512. No saline antibodies.

TABLE II

Factors in Rupture of Spleen

I. Site of extramedullary hematopoiesis
II. Increased phagocytosis
III. Weakening of supportive structures
IV. Increased intra-abdominal pressure and trauma during birth process
V. Damming back of blood from liver
VI. Increased blood volume
VII. Displacement of spleen by enlarged liver
VIII. Hemorrhagic tendency:
  A. Hypoprothrombinemia
  B. Increased capillary permeability
  C. Addition of heparin

as recommended by Weiner.[2] Blood studies of the family are shown in Table I and reveal an Rh-negative mother (rh), Rh-positive father (Rh1Rh2), Rh-positive sibling (Rh2) and an Rh-positive maternal grandmother (Rh2). Because of the multiple factors present in the cells of the father, it was concluded that he is most likely homozygous to the Rh° factor. The maternal serum revealed a postpartum rise in the anti-Rh antibody titer, which is not uncommon. Homozygosity in the father and Rh-sensitization in the mother would suggest a grave prognosis for the outcome of future pregnancies of this mating.

Table II lists the predisposing and precipitating factors to be considered in the rupture of the spleen. In erythroblastotic infants extramedullary hematopoiesis, removal of

damaged cells and damming back of the blood from the enlarged liver results in splenomegaly, congestion, and weakening of the capsule and trabeculae of the spleen. During a replacement transfusion the spleen frequently enlarges to accommodate the increased blood volume. Birth trauma may be a factor in splenic injury and it is reasonable to suppose that an enlarged, weakened spleen is more vulnerable to trivial trauma. Displacement of the spleen and laceration at the insertion of the phrenicolienal ligament has been recently reported by Gruenwald.[3] It is possible that the hemorrhagic tendency in this case was aggravated by the heparin administration.

Summary

Rupture of the spleen is reported in an erythroblastotic infant who died during an exsanguination-replacement transfusion. The changes in the spleen incident to erythroblastosis fetalis render this organ more vulnerable to trauma and rupture. The predisposing and precipitating factors include extramedullary hematopoiesis in the splenic parenchyma, increased phagocytosis, weakening of the capsule and trabeculae, increased intra-abdominal pressure during the birth process, congestive splenomegaly, hemorrhagic tendency, displacement of the spleen and the increased blood volume during a transfusion.

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Spanish Abstract

Rotura del Bazo en un Infante Eritroblastótico

Se reporta la rotura del bazo en un infante eritroblastótico que murió durante una transfusión de respuesto exanguinación. Los cambios en el bazo incidentes a la eritrobalstosis fetalis hacen este organo más vulnerable a trauma y ruptura. Los factores precipitantes y predisponentes incluyen hematopoiesis extra-medular en el bazo parénquima, fagocitosis aumentada, debilitamiento de la cápsula y trabéculas, presión intra-abdominal aumentada durante el parto, esplenomegalia congestiva, tendencia hemorrágica, desalojamiento del bazo y el volumen de sangre aumentado durante una transfusión.

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DYNAMICS OF CIRCULATION IN INFANTILE MALNUTRITION

By E. KERPEL-FRONIUS, M.D., AND F. VARGA, M.D.
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THIS study is a quantitative analysis of hemodynamics in infantile malnutrition. The leaden pallor of the skin, the lability of red blood cell counts, the cool extremities and the clinical observation that the marantic infant is an easy prey to infections are all suggestive of disturbed circulation. Certain features of these disturbances in the marantic infant were described long ago by Marriott[1] and Utheim.[2] Using a calorimetric method, they found that blood flow was significantly decreased in the extremities. In a recent study, it was found on postmortem material[3] that the size of the heart was considerably affected by the marantic process. Similar observations had been made previously by roentgenographic studies on adults in a state of semistarvation.[4]

It was felt on the basis of these facts that changed hemodynamics might be one of the limiting factors in the rebuilding of the wasted organism. To collect more information on this subject, a study was made of the blood pressure, the blood volume, the circulation time and the permeability of the capillaries in a great number of marantic infants. The data obtained are used to calculate the cardiac output, the stroke volume and the mechanical work of the heart. A possible parallelism between the work and weight of the heart, the latter obtained from postmortem material, was studied with special interest.

The accuracy of some of the assumptions used in this study may be subject to criticism. The extent of accuracy of methods used will be subsequently discussed. It is unfortunate that even some of the basic quantitative data on the function of the normal heart in infancy are not firmly established.[5]

The material studied consisted of marantic infants. The extent of malnutrition is expressed as a percentage of the ideal weight of normal infants of the same age. The "ideal weight" was calculated, for the first six months of life, as used in the routine clinical work, by the addition of 600 gm. for each month of age to the birth weight of the infant. The etiology of malnutrition in this material was due to incompetent artificial feeding with subsequent infections. Cases of infants with edema or diarrhea were excluded from this study.

RESULTS

Arterial pressure: Erroneously low values for the normal infantile systolic pressure are to be found even in textbooks. Wide arm cuffs may be responsible for low values.[5] Cuffs of 4 and 6 cm. were used in this study. The results are summarized in Figure 1.

Blood pressure: The extent of malnutrition can be read, expressed in percentage of ideal weight, on the abscissa. The figures at the extreme left are the severest cases, more than half of their body weight being wasted. The ordinate shows the value of systolic pressure in mm. mercury. The blood pressure of normal and only slightly malnourished infants ranges between 85 to 95 mm.Hg. As malnutrition progresses, the pressure declines. In the 70% group, no value above 8 mm.Hg. occurs: in the group with less than

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60% of ideal weight, all values range, with only two exceptions, between 75 to 60 mm. Hg. Blood pressure declines regularly and considerably with increasing malnutrition. In serious cases, of more than 40% underdevelopment the mean decrease in blood pressure is 25 mm.Hg.

Blood volume: Circulatory failure in infantile toxicosis is brought about by an anhydremic diminution of blood volume with simultaneous increase in blood viscosity.[1, 6, 7] This mechanism, even if not established in all clinical cases[8] is found in the majority of instances. It is, therefore, interesting to compare blood volume in relation to circulatory disturbances in infantile toxicosis and malnutrition. Marriott felt that the mechanism of

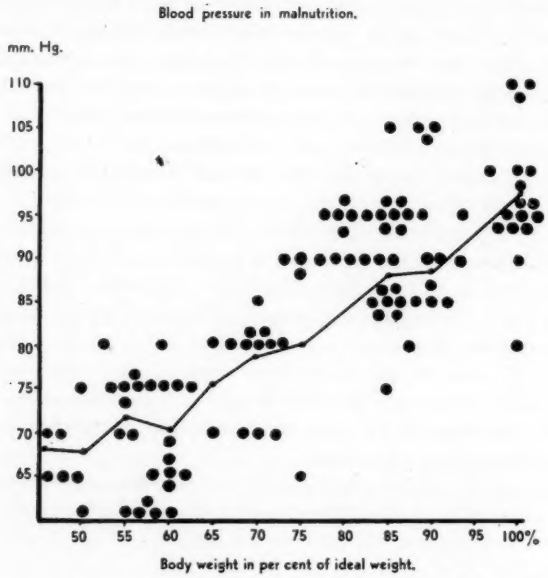

FIG. 1

the circulatory disturbance is in both conditions fundamentally similar, that is, oligemic. Evidence is accumulating, however, that blood volume is increased rather than diminished in malnutrition.[9] In this study, plasma volume was measured with Congo red dye. A solution of 1% of the dye was injected intravenously. The withdrawal of blood was made 3 to 4 minutes following the injection. Blood volume was calculated in the usual way from the data obtained and the hematocrit reading. The results are summarized in Figure 2.

The construction of the figure corresponds to that of Figure 1. The abscissa shows, when read from right to left, cases of increasingly severe malnutrition. The "normal values" were found to be 7% of the body weight, a value corresponding to that recently described by Gollan[9] using Gregersen's[10] method.

The blood volumes of malnourished infants per kg. actual weight are somewhat higher than normal, though not as high as in Gollan's material. In the severest cases, blood volume/unit body weight was frequently unchanged. This might be due to increased capillary permeability.

If the values for blood volume are related to ideal weight, the data show that blood volume is wasted to a certain extent.

Blood viscosity: Increased blood viscosity is one of the important features in the genesis of circulatory failure in toxicosis. In malnutrition, however, so far as this can be judged from the concentration of corpuscles,[11] i.e., the relation of plasma volume to corpuscle volume (Fig. 2), the viscosity does not seem to be increased.

It can be stated that the origin of circulatory disturbance in malnutrition is different from that observed in infantile dehydration.

Circulation time: The same dye was used also to measure the circulation time in the

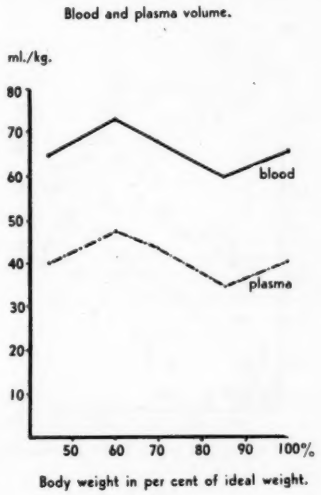

FIG. 2

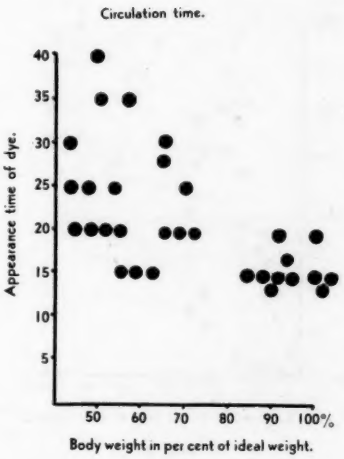

FIG. 3

marantic infants. The dye was injected in the left cubital vein, another needle being inserted simultaneously in the right cubital vein. In intervals of exactly 3 seconds, blood was drawn in heparinated glass capillaries. After the separation of the plasma from the corpuscles, the first appearance of the dye was sharply visible. The time elapsing after the injection to the first appearance of the dye in the vein of the corresponding arm is the "minimal circulation time." The latter was measured previously in normal infants. The injection of radioactive material[12] and the histamin "skin flush" method were used.[13] Using the latter, Seckel found in normal infants a minimal circulation time of 15 seconds. Our normal values are, as can be seen in Fig. 3, in close agreement with Seckel's figures.

In this figure the ordinate shows the circulation time in seconds and the abscissa the degree of undernutrition. The velocity of blood flow can be seen to be greatly diminished in marantic infants.

Cardiac Output: An estimate of cardiac output was attempted on the basis of the following calculations and assumptions: cardiac output should equal (in ml./min.):

$$\frac{\text{ml. of blood volume} \times 60}{\text{mean circulation time}}$$

The "mean circulation time" is, however, not identical with the "minimal circulation

time" as measured by us with Congo red dye. The latter corresponds only to the axial and maximal velocity of blood flow. Seckel,[13] making use of early observations of Kries,[14] following whom the "mean circulation time" approximates double the "minimal circulation time," calculated the cardiac output of normal young infants to be 165 ml./kg./body weight. This value is very near figures computed by Brock[15] and Smith[5] on the basis of oxygen consumption and surface area, respectively. Our values for the minimal circulation time are identical with Seckel's figures; the blood volume figures are, however, somewhat lower. Thus, the "normal" cardiac output of young infants was found to be 140 ml./kg./body weight. As the latter figure complies with the estimates of Brock and Smith, it

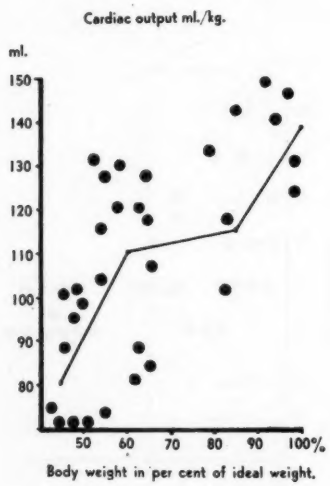

FIG. 4

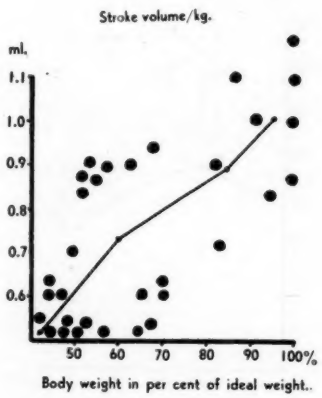

FIG. 5

would seem that our method can be used for a rough approximation of cardiac output. Figure 4 shows estimates of cardiac output in ml./kg. actual body weight (ordinate scale) in normal and marantic infants. The degree of malnutrition is to be seen on the abscissa.

The diagram shows a sharp decline in cardiac output parallel to increasing malnutrition. Figure 5 shows the same to be true for the "stroke volume" $\frac{\text{(cardiac output)}}{\text{pulse rate}}$.

The pulse rate did not decrease in the malnourished infants. Bradycardia, on the other hand, is a constant feature of starvation in the adult.[4]

Cardiac output is believed to be more closely related to surface area than to body weight (Fig. 4). This fact is the reason for the high cardiac output per kilo of body weight of the infant. For this reason, in Fig. 6, the data for cardiac output is presented per unit of actual surface area.

Figure 6 shows that cardiac output per square meter of surface area falls rapidly as malnutrition progresses.

Cardiac weight: In Figure 7 the physical work of the heart was related to the cardiac weight of marantic infants.

The abscissa shows the degree of malnutrition. The ordinate shows the degree of wasting of the hearts. The cardiac weights of marantic infants of the postmortem material are

shown in per cents of weight of hearts of normal infants of a corresponding age. The normal figures are taken from Copoletta and Wolbach's[16] growth curves. It can be seen that with increasing malnutrition the cardiac weight of marantic infants represents an ever decreasing percentage of the cardiac weight of normal infants of a corresponding age.

There has been added to this figure, showing as mentioned above, the progressive

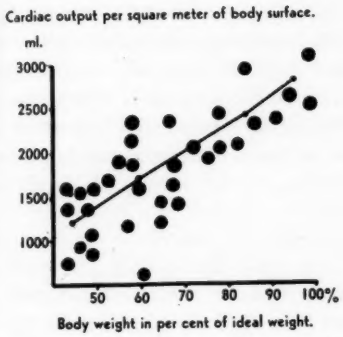

FIG. 6

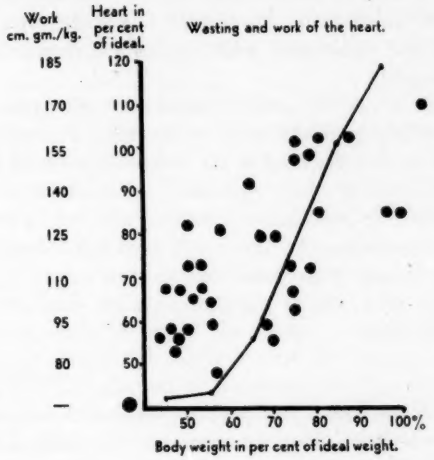

FIG. 7

decline of cardiac weight in malnutrition, the mean values for the physical work of the heart. The latter was calculated in the usual way from systolic pressure and stroke volume of the living marantic infants. The close parallel between wasting and decline of the work of the heart per unit body weight is clearly visible.

A similar relation between the physical work of the heart and its size, as measured on roentgenkymograms, was recently described in semistarvation of the adult by Keys, Henschel and Taylor.[4]

Capillary permeability: In severe cases of malnutrition, using the method of Landis,[17]

TABLE I

Age in mos.	Weight gm.	Weight in per cent of ideal weight	Amount of escaped fluid	Protein content of escaped fluid	Serum-protein
10	3550	41%	28 ml.	4.66%	4.58%
9	3450	43	14	4.02	5.77
9	3450	44	11	5.13	6.88
8	3700	47	18	6.01	7.11
9½	4870	55	15	4.10	6.71
3	3400	65	4	0	6.45
3	2750	66	4	0	6.46
2	3370	70	0	0	6.58
4	5640	85	0	0	7.69
4	5200	91	0	0	6.80

a greatly increased permeability of the capillaries was found. A pressure of 30 mm.Hg was applied on one arm for 30 minutes' duration. The results are summarized in Table I.

The table demonstrates that in severe cases of malnutrition the capillary membrane lost its semipermeability; the escaped fluid is nearly as rich in proteins as is blood plasma. In less serious cases of malnutrition, no abnormal fluid escape could be detected. Gollan,[9] in a series of malnourished infants, described an increased disappearance rate of T—1824 dye. Gömöri and coworkers[18] found that after the siege of Budapest a large number of the semistarved adult population showed an abnormally increased capillary permeability.

It is not the primary purpose of this paper to analyse the importance of increased capillary permeability in malnutrition. It should be mentioned, however, that the first three cases described in the table were edematous, while serum protein values were above the level at which appearance of starvation edema might be expected. On the other hand, the abnormalities observed may have a bearing on the accuracy of blood volume determination. An abnormally accelerated disappearance of injected dyes may result in erroneously high blood volumes. Last but not least, increased capillary permeability may lead to a loss of circulating plasma thus contributing to the severity of circulatory disturbance.

Comment

It was found in a previous work[3] that malnutrition does not affect all the organs of the body in an equal measure. In the malnourished body, the relation of the weight of individual organs to body weight is greatly changed; fat and muscle tissue are extremely wasted, while the central nervous system and the kidneys are only slightly affected and the body surface moderately. The heart was found to be one of the greatly wasted organs, its weight loss approximating that of the body as a whole. The malnourished infant, if compared to a normal infant, has consequently per unit of body weight a brain almost twice the size, large kidneys and a great body surface. As the organs mentioned above claim an important part of the cardiac output, and, on the other hand, the heart is wasted, there may result a disparity between supply and demand of blood. How far this disparity is balanced by the wasting of muscle tissue cannot be answered now.

Malnutrition strongly affects muscle tissue, i.e., the system containing the largest proportion of intracellular fluids of the body. On the other hand, the skin (body surface) and central nervous system (the systems containing a higher proportion of extracellular than intracellular fluids) are increased per unit of body weight. This disproportion in wasting leads to an increase of extracellular and decrease in intracellular fluids per unit of body weight.[19, 3] Thus, in rehabilitation after malnutrition, the need for new protoplasmic tissue is even greater than indicated by the mere extent of weight loss.

The new composition of the malnourished body described above is similar to that of the premature baby. A body with such proportions, be the exact cause of it immaturity or wasting, contains a high amount of extracellular fluid and requires a high caloric and protein intake.

The circulation of the marantic child is, however, as has been pointed out, on the margin of circulatory failure. Thus, attempts to meet excessive energy requirements may result in weight loss and diarrhea, the "paradoxical reactions" of Finkelstein.[20]

The course which infections take in the malnourished body is influenced equally unfavorably by the poor circulation. Shock or pneumonia may easily develop. Briefly,

the state of circulation in infantile marasmus seems to be one of the limiting factors in rehabilitation and one of the causes of the frequently fatal outcome of complicating banal infections.

It is interesting to note that the disturbance of circulation, i.e., the decrease in the physical work of the heart and the increased permeability of the capillaries, take on really serious proportions when body weight is wasted to more than 35% of the ideal weight. This extent of malnutrition was known to the older pediatricians as "Quest's figure." It was believed that if more than one third of the ideal weight was wasted, recovery would be impossible.[21, 22]

Of course, modern therapeutic measures—the use of intravenous plasma, a larger percentage of carbohydrate in the high caloric diet, penicillin in intercurrent infections—have allowed the rehabilitation of cases which have wasted to more than half the ideal body weight. The fact still holds true, however, that clinical difficulties usually begin at a degree of wasting of 30 to 35% of the ideal weight and this degree of wasting coincides with the appearance of signs of poor circulation.

Summary

Hemodynamics in marantic infants were found to be on the margin of circulatory failure. Signs of disturbed circulation appear usually at a degree of wasting of more than 30% of the ideal weight. The condition is characterized by decreased blood pressure, cardiac output, stroke volume, by a longer circulation time and by increased capillary permeability for fluids and protein. Blood volume appears to be somewhat increased. A decrease in the physical work of the heart was found to be parallel to the wasting of the latter. Inequality of wasting of different organs results in a large brain, kidneys and body surface per unit of body weight, in contrast to an atrophic heart, and atrophic muscle system. The possible consequence of changed body proportion to circulation is discussed. The origin of circulatory disturbance in malnutrition was shown to be different from that observed in infantile toxicosis. The state of circulation in infantile marasmus seems to be one of the limiting factors in the rebuilding of the body and one of the causes of the high fatality rate following intercurrent banal infections.

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SPANISH ABSTRACT

La Dinámica de la Circulación en la Desnutrición Infantil

En infantes marásmicos aparecen signos de circulación alterada generalmente a un grado de desgaste de más del 30% del peso ideal. La condición se caracteriza por presión arterial reducida, rendimiento cardiaco, volumen de golpes, por un tiempo de circulación más largo y por permeabilidad capilar para flúidos y proteina. El volumen de sangre aparece algo aumentado. Esta disminución en el trabajo físico del corazón se encontró paralela al desgaste del último. La desigualdad de desgaste de los diferentes organos resulta en un cerebro grande, superficie de cuerpo y riñones por unidad de peso de cuerpo, en contraste con un corazón atrófico y sistema muscular atrófico. Se trata de la posible consecuencia de proporciones cambiadas del cuerpo a la circulación. Se demostró que el origen del desorden circulatorio en la desnutrición es diferente al que se observa en toxicosis infantil. El estado de circulación en el marasmo infantil parece ser uno de los factores limitantes en la reconstrucción del cuerpo y una de las causas del tipo de alta fatalidad después de infecciones intercurrentes triviales.

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PSYCHOLOGIC ASPECTS OF POLIOMYELITIS

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INTRODUCTION

PROBABLY no one of the medical specialists has reason to be more keenly aware of the psychologic elements in the care and treatment of the patient than the pediatrician. The constant contact which he maintains with the child and parent serves to remind him continually that ills of the body run concurrently with and often amplify the psychologic problems of adjustment.

Chronic or acute illness may be looked upon in reality as an environmental complication which the child may or may not be prepared to accept. Depending largely upon his capacity to tolerate the newly imposed psychologic stresses resulting from his illness, the sick child will continue at an emotionally even keel or will be storm-tossed upon the Sea of Insecurity. Pediatricians are frequently called upon to rescue the patient who sends out psychic SOS calls which are transmitted in the code forms of tears, situational depressions, temper tantrums and the like.

The topic presented in this discussion, which has received some coverage in the literature,[1-11] is rather specifically delimited to the psychologic elements commonly encountered in caring for the patient with poliomyelitis. It seems justifiable to point out, however, that essentially the same facets of behavior may readily be seen in any disease which has an acute onset, a prolonged convalescence and at least the threat of permanent physical disability. It is hoped that those who deal with diseases such as tuberculosis, diabetes, arthritides, and cardiac disease will find concepts that will be as useful to them as to those treating the patient with poliomyelitis.

The splendid contributions of such experts in pediatric psychology as Gesell, Ilg, Armatruda, Bakwin and Spock, to name but a few, make it unnecessary to dwell upon the basic problems of behavior in the normal child. Fundamentally, the child with poliomyelitis who was essentially normal prior to the onset of this illness may be represented by at least the following elements: (1) the acute effects of the disease (toxicity); (2) the effects of his environment (institutionalization and care); (3) the effects derived from the child's concepts of his illness; (4) the effects of the parental reaction to the child and his illness; (5) the effects of the child's social community upon him and the sequelae of his disease. These five elements, therefore, will be considered individually at this time.

PSYCHOLOGIC PROBLEMS OF THE ACUTELY ILL CHILD

The symptomatology of poliomyelitis is subject to a great deal of variation in its febrile course, in the extent and degree of resulting paralysis and in the localization of nerve cells injured and destroyed.

From the National Foundation for Infantile Paralysis, New York, N.Y.

Read at the 17th Annual Meeting of the American Academy of Pediatrics, Atlantic City, N.J., Nov. 21, 1948.

(Received for publication Nov. 3, 1948.)

We find the preparalytic phase characterized ordinarily by fever and a gradually to rapidly increasing central nervous system involvement. Paralysis, when it occurs, often begins on the third to fifth day. By the fifth to seventh day temperature has frequently dropped to normal (75% of cases).

In the so-called "dromedary" type, a period of illness of two or three days generally characterized as without specific neurologic symptomatology is followed by from one to four days in which the patient is essentially symptom free. This is followed by a secondary temperature rise which then continues much the same as that described in the ordinary febrile course (25% of cases).

Headache, nausea and vomiting are frequently associated with the preparalytic stage. Pain is often present and may be severe.

These symptoms unquestionably make a contribution to the psychologic reaction of the patient. The extent of this reaction is influenced largely by its severity and the preparedness of the patient for what is occurring.

The clinical psychologic findings in the acutely ill child with polio or, as a matter of fact, in any illness with similar symptoms, are initial reaction to pain and noxious stimuli to be followed later in some instances by reactions of fear relative to the disease after the patient has become aware of its paralyzing effects and its other sequelae.

If the child has been emotionally stable prior to the onset of the present illness and if the general family situation was one which could be considered as psychologically healthy, we may anticipate a minimum of difficulty in carrying the child through this phase of his illness. Usually all that is needed beyond the normal procedures for reduction or alleviation of pain and other symptoms of the disease is a brief explanation of any perplexing elements in the environment by the physician and augmented by the nurse and physical therapist.

It is more rare than we care to admit, unfortunately, that we find a child sufficiently calm and well-oriented emotionally to permit this rather cursory handling. Frequently the isolation, coupled with various rather heroic treatment procedures, tends to introduce many elements capable of producing fear. When we are dealing with individual children entering the hospital for acute care the problems can be (but often aren't) promptly and easily dealt with. When, however, we are confronted with the epidemic situation with patients literally pouring into the hospital by the dozens as has been true in many states this year, it is a most difficult task to get to these children with prompt psychologic help. Yet, in many instances, what happens to the child during the first 10 days to two weeks may do much to determine the kind of adjustment he will make throughout the course of his illness and convalescence and often may play a role even in his total post-polio adaptation to life.

Inasmuch as the situation during the acute phase of the disease is subject to great variation as is also the medical care situation, one can only offer rather general suggestions as to what should be done to reduce or, better yet, to minimize the psychic stresses of this trying period. These include:

(a) Prompt and adequate explanation to the child of the facts he needs to know about his illness and the method of treatment. This should be given only by the physician or a qualified person properly oriented to the facts about the patient. It includes providing the patient with the opportunity to ask questions and receive answers to problems which trouble him.

(b) Prompt contact with parents and relief of their fears and guilt feelings regarding

their responsibility for the child's illness. Matters of treatment technic, isolation practice and parent-child relationships as they apply to the patient should be made clear.

(c) Prompt orientation of the staff personnel regarding the specific patient, including provision for the psychologic as well as the physical comfort of the child.

Once these three things have been dealt with successfully, the patient generally will proceed through the acute phase with minimal difficulty in adjustment. In rare instances specific behavior problems may arise which require more urgent and extensive handling. These can be met by use of a consultant trained in child psychiatry or psychology when available.

Mention has not been made of the more serious complications arising from bulbar and polio-encephalitis. Obviously both types of pathology create much more severe psychologic problems. The only suggestion that can be made is for the amplification of the program in the care of the patient requiring the respirator to include prompt and clear explanation of the respirator and its functions. The process of weaning the patient from the respirator begins from the first moment he adjusts to it and does not cease until he remains out of it for the maximum period feasible. By adopting such a philosophy, close attachment of patient to respirator is minimized.

The problem of emotional adjustment and mental status of the patient with an established encephalitis must be dealt with as early as safety will permit. Recognition of the effects upon the brain as evidenced in behavior patterns of the child is necessary. Appraisal of brain damage will of course be postponed until after subsidence of the fever and the completion of the acute process but should then be begun so that temporary deterioration as well as permanent damage can be evaluated and a base line for improved behavioral functions can be established.

Whenever possible, adequate use of medical social workers is desirable from the standpoint of both the patient and his family. When a medical social worker is present, she can provide the frame of reference around which an evaluation of the patient's present status is to be based. In addition, her role in dealing with the patient, parent and community, as well as her normal liaison services in coordinating and protecting the patient's best interests can hardly be over-estimated.

The principal point to be kept in mind in meeting the psychologic problems of the patient during the acute phase of polio is that "an ounce of prevention is *truly* worth a pound of cure." The prevention of excessive mental stresses and emotional disturbance during the acute and early convalescent phases will do more to help the patient emerge without mental sequelae than any other procedure.

Environmental Factors Affecting the Sick Child

The patient, once he has emerged from the acute phase of poliomyelitis, starts a more or less prolonged period of convalescence. If the child comes through the acute phase with essentially no residuum or if the residual paralysis is minimal, then one may expect to have the problem of keeping an otherwise healthy child under a rather rigid program. This program would call for physical therapy and other more routinized treatment which confines him to bed. Depending upon the degree to which he is limited in the freedom of activity, the child may be expected to become restless, resistant to treatment and noncooperative.

Here, as in the acute phase, it would appear desirable to supply the child with an orientation regarding his convalescent program, an explanation (repeated as necessary)

regarding the need for rest periods, limitation of activity, and the like. If couched in an understandable vocabulary, this will motivate him toward a more cooperative role in treatment.

Even under the most favorable circumstances, we can expect at least a moderate tendency for the child to show emotional retrogression when he is ill for a prolonged period. It is highly important, therefore, that parents as well as all medical personnel be oriented to the necessity of insisting that the child be helped toward independence and self-motivation. At the same time egocentricity must be minimized. This requires training the child to take care of his own needs as far as he is physically capable and within the limits recommended by the orthopedist, the psychiatrist and/or the physical therapist.

All too frequently these specialists become so absorbed, unfortunately, in the physiologic task of returning function to an affected part or in the development of substitute motions where function cannot be returned to the normal part that they forget the necessity for integrating these functions into the total normal behavior pattern of the child. Thus, in prescribing a program for physical and psychologic reorientation, it is essential that provisions be made to integrate these functions that the child was accustomed to perform for himself prior to the onset of his illness. This will need to be re-enforced by making clear to the parents that such activities are necessary and essential for the child's ultimate recovery.

While it is fortunate that most children are going to be free of residuals or have only minimal residuals, there always will be about 25 to 35% rather badly hit by the virus.

Such children obviously, in addition to having all the psychologic problems of the non- or minimally-residual group, will have all the fears engendered by their concepts of how the residua are going to interfere with their lives.

This is usually further complicated by the rather severe reactions which parents are likely to develop when they learn that their child is to be more or less severely disabled.

What can be done to prevent or at least alleviate these psychic traumata is the most difficult psychologic problem with which one has to deal in pediatric psychology. Since it is associated intimately with the orthopedic problem, it is likely that the orthopedist will be the one who must deal with it initially. It certainly would be well advised for the physician, however, to be completely aware of what the orthopedist has indicated to the patient and his parents.

Actually what the orthopedist tells the patient will depend upon (a) the extent to which the recovery of function has proceeded; (b) the degree to which the temporary inhibition of neuro-muscular function can be differentiated from permanent damage; (c) the philosophy of the orthopedist regarding the frank and complete statement of physical status; (d) the surgical program planned, and (e) prosthetic support required and obtained.

It is desirable under any circumstances for the patient to have as clear a concept of his physical status as possible, given as promptly as consistent with the orthopedist's professional judgment. If in addition to appraising the patient's deficits there can be included (as there should be) an appraisal of his physical and mental assets, coupled with a plan which includes a résumé of the plan for physical, educational and social reorientation, there is a fairly good chance that the patient and those who are caring for him will move toward complete rehabilitation promptly.

Obviously where the patient has been left more or less to "stew in his own juice" we may expect to find a psychologic problem of no mean dimensions awaiting the physi-

cian when the patient returns to his care. Perhaps this problem can be reduced if the physician can assume some of the burden of explanation and orientation of the patient during the period he is undergoing orthopedic rehabilitation. If there is any justification for the medical team concept, here is a place where orthopedist and physician surely can do a great deal for the patient if they play a closely coordinated game.

The patient's parents, similarly, must be given an adequate understanding of their child's orthopedic problem. They need to know what the child can and cannot do; what surgery may be necessary ultimately and when and what type of prosthesis will be necessary. Furthermore, if they have any archaic, nonsensical or psychologically harmful ideas regarding disabilities the time to correct them is not after the child has gone home and is being exposed to the effects of these ideas during all of his waking hours but rather early in the game before the child is traumatized by them.

This is a place once again where orthopedist and physician can well afford to link arms and tackle the job of parental orientation.

Furthermore, the medical social worker is a most valuable team member in dealing with the patient and parents from the standpoint of clarifying many questions, alleviating fears, and in coordinating the plan designed to return the patient to a normal life.

There are other environmental factors beside his orthopedic problem which affect the patient during the convalescent period. These include such problems as nostalgia, reaction to "limelight," sibling-rivalry status, educational needs, need for emotional outlets and many others. While space will not permit dealing with these at length at least three of them deserve some further emphasis.

There is a desire on the part of most of us to "bask in the limelight." In children this is frequently present when there is a felt need for attention. When, however, the child is ill the need for ego-support is greater but at the same time the tendency to focus attention on the sick child is much greater than is true for most healthy children. As a result the child who is hospitalized may become increasingly egocentric the longer he remains in that situation. When, however, the child has been suffering marked ego-deprivations prior to the onset of his illness, such as occurs when younger siblings siphon off parental interest, the satisfactions arising out of the rebirth of parental interest coupled with the ego-satisfactions obtained from the hospital staff may overwhelm the child and create the severe loss of discipline frequently observed in the polio child. This is fundamentally a situational phenomenon which can be greatly reduced in severity if parents and staff are forewarned against it and properly oriented regarding the lasting disorientation and emotional distress that may follow upon its heels unless proper precautions are observed.

Another factor which merits attention is the need which the patient has for attention to a program of useful employment of time while in the hospital and during institutional or home convalescence. Useful employment of time for children implies that during those periods when the child is not actually undergoing treatment his mind is active and he has motivational drives which vary in intensity but which are present to some degree in all children. When not properly recognized and provision made for their utilization these drives force the child into overt behavior that is frequently annoying, often harmful to physical recovery and psychologically wasteful.

When we recognize that a high percentage of children (at least one third of the children without physical residuals and up to two thirds with residuals, in studies made thus far) with poliomyelitis are one or more years school-retarded and many fail to

maintain the proper social relationships established ordinarily in the school and playground, it behooves us to consider the necessity for supplying both adequate socialization and educational opportunities for these children. There is no reason thus far revealed which justifies, in the vast majority of cases, the loss of schooling or of maintaining proper social attitudes among these children.

We have failed to recognize this factor as an important element in medical care. We must ask ourselves, "What does it profit us to strive to reduce and ultimately eliminate physical limitation if we are to create psychologic disabilities that may be as great or greater handicaps?"

The introduction of a suitable educational program into the convalescent period can do much to reduce tensions, embarrassment, and similar reactions and at the same time prevent the child from losing contact with reality. Further, it furnishes a clue which will indicate the increase in physical and psychologic stamina, initiative and motivation.

While schooling is important for school-age children we must not overlook the needs of preschool children for mental stimulation and socialization. Here intelligent use of parents and volunteers can make it possible to provide these younger patients with the kind of psychic support they need.

A third and final factor to be considered is the grave need of the child with poliomyelitis for the support that comes from love and understanding. Some of the fears of these children are founded upon their lengthy exposure to the highly organized efficiency of a hospital program. Necessary as such efficiency may be, it is even more necessary that the child does not develop the impression that the polio virus has dropped him into a cold and indifferent world.

Some may consider this point as a paradox when compared with what has already been said as a warning against over-indulgence. In reality this is no paradox whatever—for love and affection shown by a warm, wholehearted understanding of the child's problem is not over-indulgence. But the indifference which permits excessive license, freedom from proper discipline and the "bribery" of unreasonable gift-giving definitely are indications of over-indulgence.

Every physcian and orthopedist owes it to his patient to prescribe "TLC" (tender loving care) *ad libidum* and to see to it that all hospital personnel and parents administer it regularly and continuously. They'll need that feeling of security when they start bucking a cold, material world.

The Child's Concept of His Illness

It is important that the physician and the orthopedist recognize that, as a rule, the child knows little about poliomyelitis beyond what he sees, hears and gathers intuitively. Because generally the sources of his information are unscientific, inaccurate and often highly exaggerated, it is hardly surprising that much of the psychologic reaction to his illness is based upon fallacious reasoning.

Since such misinformation engenders fear and emotional reactions distinctly inimical to the patient's health, it is a medical responsibility to ferret out the patient's erroneous concepts and correct them. This process should be accomplished, if possible, from the onset or at the earliest possible moment so that the harmful effects are minimized.

To accomplish this will seldom require more than providing the child with an opportunity to ask questions and talk about his annoyances, worries and grievances. After he

has "let his hair down" he should be provided with the proper and correct orientation in a language which is intelligible to him.

This requires the cooperation of the entire medical staff, with particular emphasis on the part played by the physician, the medical social worker (when present), the nurse and the physical therapist.

A patient who is allowed to worry or become apprehensive about nonexistent events or eventualities is being encouraged to become maladjusted. A little effort spent in orientation toward the facts can turn this situation into an intelligent phase of medical care.

Later, as the care of the patient progresses, new problems related to capacities and potentialities will arise to plague him. They too will need prompt recognition followed by equally prompt correction.

Too frequently we are inclined to take for granted the idea that the patient accepts his lot philosophically, especially when his doctor says by word or implication, "Don't worry, I have everything under control." Occasionally one may find adults who do accept this point of view. Far less often, probably, than is the fact. But when it is seen from the standpoint of the child, we must recognize that physician and patient have such entirely different backgrounds of experience that the child must view the events in physical care from an entirely different vantage point than does the doctor. Obviously there can be little understanding of the meaning of the therapeutic program. All the child knows is that he's afraid, alone, in a world peopled by individuals with sharp needles, peculiar instruments of varied sorts which often inflict pain and discomfort.

To the extent that one is able to place the child at ease, relieve his fears and return to him the sense of security that makes for mental comfort the patient will gain in psychologic as well as physical health. To the extent the small patient understands the "what, why and how" of his illness and the treatment thereof, one will secure his cooperation in the program he is expected to follow. In poliomyelitis, cooperation on the part of the patient is particularly important since physical therapy can seldom be accomplished successfully without his willingness to participate wholeheartedly. So too the preparation of the patient for surgery, for prosthesis and for the necessity of learning to live with his physical liabilities constantly competing with his psychologic assets is fundamental.

The Parents' Reactions to the Child's Illness

As important as the child's reaction to his illness, and sometimes even more significant in influencing his behavior, is the reaction of the parents to the disease as they see its role in the life of their child.

There are many responses which parents may have. At first one may anticipate the panic which is often seen when the child, more or less abruptly, is removed to isolation. There is likely to be a tremendous emotional upheaval as the parents hear the dread words "infantile paralysis." They immediately picture in their mind's eye a child almost completely encompassed in the maws of the awe-inspiring respirator or the later, but no less terrifying, picture of a child completely encased in their fantasied concept of braces, wheel chair and crutches.

Then there are other fears. Fears about contagion, in which other siblings come down with the dread disease. Fears, generally unexpressed, that they, the parents, may become

victims of the virus. Fears that their neighbors and friends will be afraid of them. Fears that their child will be a helpless, hopeless invalid. And finally the most awful of all fears—the fear that they may have, through carelessness, allowed their child to be exposed to the virus of polio and have thus been responsible for the unhappiness they anticipate will be the lot of their beloved forever.

Whatever the details, whatever the pattern of the psychic anguish, the parents need help, mostly in the form of down-to-earth explanations of the facts. They need to be relieved of feelings of guilt, of the mental aberrations built out of old wives' tales and false concepts. Above all they need to be oriented toward their responsibilities and the part they must play in helping their child maintain a wholesome, stable emotional attitude; realistic but not lacking in hope; determined but not cynical and distorted. With the parents rests the decision, to a large extent, whether or not their child will emerge from polio with a psychic residual or with a normal, healthy determination to go on with his aims and attain his goals.

Much of the orientation of these parents must, of necessity be derived—or fail to be derived—from the physician. As a rule the doctor, who has taken care of the child in many periods of illness and in health as well, has the confidence and trust of the parents. When the child goes into isolation, the physician is the one best suited to explain clearly to the parents just what this period means; why the parents cannot see their child during this period; the preparation of the parents for their role in the convalescent period; the orientation of the parents to the probable orthopedic situation and the physical therapy program that will be required.

These and many other elements will be present as problems which the parents will discuss with the physicians if given the opportunity. In poliomyelitis and in many other diseases this step in preventive mental hygiene is fundamental to the mental health of the patient.

The Community Reaction to the Child with a Residual Disability

Difficult as the trials for patient and parents may be during the acute and convalescent stages of polio, the readjustment as a rule will be relatively easy if the patient is left without a residual disability or with a disability so mild and limited in extent that it is generally invisible to the casual observer.

About 75% of polio patients manage to emerge, fortunately, with such a recovery result. But there are always some 15 to 20% who are left with residua varying in severity from those who will ultimately require major reconstructive surgery, extensive prosthetic support or a combination of both, to those who must spend the major portion if not their entire time in bed or in a respirator.

What can be done psychologically for this group of patients obviously is subjected to a great deal of variation. At best, when motivation is strong and courage is high the patient can be prepared to carry on most of the steps necessary to attain a rather high degree of independent action. In this sort of patient it is often possible to provide training which will equip them to carry on a useful and satisfying socio-economic adjustment to living.

The attainment of self-reliance and independence of action is proportionately less in those patients less motivated and more lacking in intact mental and physical assets. Whatever the situation, the medical obligation is to provide the stimulus and the

opportunity for the attainment of as nearly complete and total rehabilitation as possible. In many places today serious effort is being made to accomplish this goal.

There is, however, a catch to the successful accomplishment of this aim. No matter how great the opportunities for training, how intensely we work to maintain the patient's courage and motivation, and no matter how successfully the capacity for socio-economic independence has been developed, the patient must frequently lose out since his society is not prepared to accept him in terms of his assets but prefers to beat him down into hopeless social invalidism because he has been refused the opportunity to attain his effective level of performance.

Busy as the physician is with his ordinary and regular professional obligations it is highly desirable—essential, as a matter of fact—that he utilize his influence in his community to secure more complete understanding of the child and his disabilities. It is, for example, essential that school boards and superintendents be educated to the necessity of establishing suitable educational opportunities for the orthopedically disabled as well as the orthogenically retarded child.

Not only is the provision of suitable hospital and home-bound education necessary, but there is also a need for establishing good educational opportunities in the regular schools for most of these children—the latter being in contrast to the growing tendency to set up "special" schools for handicapped children. An occasional school of this type may be essential for those so severely afflicted that no one can anticipate their assumption of a place in a regular competitive vocational or social situation.

Our aim in the rehabilitation program, actually, is to return the individual to a regular normal socio-economic sphere rather than to one in which all sorts of special considerations are to be made. With such a philosophy the child is viewed as an individual who, like most of us, has some limitations but makes good in terms of his capabilities rather than on the basis of special privilege. Obviously, then, such a child needs his training in the environment in which all other normal children are trained. Often this can be done for the orthopedically limited by the simple provision of elevators or ramps which permit easy access to class rooms.

The emphasis on the point-of-view of a normal environment for the education of most physically limited children, in contrast to the "special school," needs the support of the physician who can make the rationale of this attitude clear to the laity. He, in company with the orthopedist and psychiatrist, the medical social worker and the psychologist, can be of tremendous influence in reorienting the community on this important matter.

Again, the physician can do much to explain poliomyelitis to his community, to eliminate gross and harmful misconceptions, and can make clear the known facts about the disease, its treatment and after-effects. Above all he can emphasize the point that the harm which this virus may produce in the patient can be greatly reduced if the community recognizes that its responsibilities are not discharged by economic support of the campaign against this disease but must also extend toward a helpful and understanding cooperation in returning the boy and girl with polio residuals to their rightful places in their society.

Conclusions

While many more contributions may be made by the physician in caring for the child with poliomyelitis there are at least five principal areas in which he plays a major

psychologic role in addition to his ordinary responsibilities in regard to medical care of the patient. These are:

(a) in dealing with the relief of the patient's psychologic reactions to the acute phase of the disease; (b) in reducing psychologic trauma attendant upon the removal of the patient from his normal environment and placing him in the treatment environment of the hospital or nursing institution; (c) by explaining and correcting misconceptions that the patient may have about his illness and its ultimate effects; (d) by aiding the parents to avoid erroneous concepts, feelings of personal guilt and improper attitudes toward their child and the family as a whole during the child's illness; and (e) by correcting community misconceptions regarding the needs of the child with polio and by fostering adequate community cooperation in helping disabled children make the best possible socio-economic and psychologic adjustment to life.

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Spanish Abstract

Aspectos Psicológicos de la Parálisis Infantil

Las enfermedades que incapacitan al enfermo, tales como la parálisis infantil, suelen recibir gran atención en lo que atañe a sus efectos físicos. No obstante, los efectos psicológicos producidos directa e indirectamente por esas enfermedades son tan perturbadores para el niño y sus padres como los cambios físicos que ocasionan.

De ahí que deba prestarse especial cuidado a las normas de higiene mental preventiva, para resolver los problemas anejos a las enfermedades agudas que inhabilitan al paciente.

El autor enumera los efectos psicológicos más importantes que tienen su origen en la parálisis infantil, y explica varios métodos mediante los cuales pueden impedirse o aliviarse esos efectos.

120 Broadway

INFLUENZAL MENINGITIS; RECOVERY OF A CASE OF FOUR WEEKS' DURATION WITH THE USE OF A NEW DRUG, POLYMYXIN B (AEROSPORIN)

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NOT long ago, almost all infants with influenzal meningitis died. In 1937, Fothergill[1] reported that 31 of 201 patients with the disease recovered when they were given specific horse anti-influenzal serum and complement (mortality 84.6%). A few recoveries were reported following the introduction of sulfanilamide in 1936. Sulfapyridine and sulfadiazine successively were each found to improve the recovery rate. With the introduction by Alexander in 1939 of specific rabbit serum for type b H. influenzae, the mortality rate dropped further.[2] In 1943, she reported 57 recoveries out of 75 cases (mortality 26%) using specific rabbit anti-influenzal serum combined with a sulfonamide.[3]

In 1947, Alexander and Leidy[4] reported that "virtually 100% of these patients recover when treated with streptomycin and specific rabbit anti-influenza serum within a few days of the onset of illness." Levinson[5] has obtained similar results with a combination of streptomycin and sulfadiazine. Such progress in therapy of a previously highly fatal disease in little over a decade is impressive.

This report of a case of influenzal meningitis is made because streptomycin combined with sulfadiazine did not effect a cure, because the delayed administration of specific rabbit anti-influenzal serum also did not save the infant, and because cure was effected by means of a new drug, polymyxin B (aerosporin).*

The diagnosis was made early, and streptomycin and sulfadiazine were used in large doses. After two weeks when progress was unsatisfactory the infant was transferred to our hospital where streptomycin and sulfadiazine were continued, and in addition Alexander's specific rabbit anti-influenzal serum was given. When the child had had meningitis for four weeks and a fatal termination seemed inevitable, at a time when the spinal fluid culture showed a relatively heavy growth of type b H. influenzae, and the spinal fluid glucose was zero, he was given polymyxin B with a most remarkable recovery. The prognosis of this disease in a 13 month old infant when present four weeks after the onset and with the absence of detectable glucose in the spinal fluid is extremely poor with any therapy.[6] It should be noted, however, that Alexander[7] reported one case (P. H.) of meningitis due to type b H. influenzae in a 4 year old child who recovered after an illness of about five weeks following persistent therapy with specific rabbit anti-influenzal serum and sulfadiazine.

Polymyxin A was first reported in England by Ainsworth, Brown and Brownlee[8] in 1947. At about the same time a related antibiotic now known as polymyxin D was

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reported by Stansly, Shepherd and White[9] in this country. Both are derived from Bacillus polymyxin. They are principally basic polypeptides plus a fatty acid component. Polymyxin is stable in the dry state at room temperature. The standard of reference is a polymyxin A hydrochloride of high chemical purity, containing 10,000 bioassay units of antibiotic activity per milligram of dry substance. According to Brownlee and Bushby,[10] it is bactericidal rather than bacteriostatic. There has been little evidence of the development of resistant strains. Against H. influenzae, polymyxin A was reported to be 50 times as effective as streptomycin in terms of micrograms per cc. of medium. Schoenbach et al.[11] reported that polymyxin D could not be detected in the spinal fluid of dogs in which high serum concentrations of the drug were present. They also found that 5 mg. given intrathecally produced no untoward reactions, while 10 mg. produced transient paresis of the hind legs. With this experimental data in mind and because the infant in the case reported in this paper was so critically ill, part of the drug was administered intrathecally in the dosage noted below.

Case Report

J. C. was a 13 mo. old white male infant weighing 8.4 kg. on admission to Sarah Morris Hospital. Four wks. before admission to this hospital he developed a purulent otitis media on the left side which persisted for 2 wks. Two wks. before admission, he had been taken to another hospital because of fever and a convulsion. Apparently little significance was attached to the findings because he was given an enema and sent home. His fever continued, and that evening he became unconscious and had more convulsions. He was taken back to the hospital and admitted. At the time of admission, he was still having convulsions and was unconscious. Respiratory rate was decreased; neck was stiff; left ear drum was red; pupils were fixed and dilated; temperature was 39.4°C. Lumbar puncture at that time revealed a pressure of 350 mm. H_2O and yielded "milky" fluid. Spinal fluid white cell count was 8.75 thousand/cmm.; glucose was 11.7 mg./100 cc. Culture revealed H. influenzae organisms. On admission to that hospital, he was given streptomycin 0.5 gm. intramuscularly followed by 0.25 gm. every 3 hrs. (total of 2 gm./day); sulfadiazine 3 gm. was given daily by mouth (approximately 0.3 gm./kg./day); sodium penicillin G 20,000 u. in saline was given intramuscularly every 3 hrs. The infant was kept in an oxygen tent. The response seemed to be good. Temperature became normal and consciousness returned. Roentgenograms revealed a "suggestion of pneumonia in both upper lobes" and "some inflammatory reaction in the left mastoid." Therapy was continued for 1 wk., at the end of which time his spinal fluid was clear; there were 115 white cells, mostly lymphocytes; glucose was 36 mg./100 cc.; no bacteria were found on direct smear. Blood sulfadiazine concentration was reported to be 25.5 mg /100 cc. Because he developed hematuria, sulfadiazine was discontinued. Penicillin was continued. The dose of streptomycin was dropped to 0.125 gm. every 3 hrs. (total of 1 gm./day). Soon thereafter, he developed fever and appeared to be worse. Three days before transfer to our hospital, he began to vomit and was irritable. His fever continued and his neck became rigid. Two days before transfer, spinal fluid pressure was 310 mm. H_2O; white cell count was 800; glucose was 30 mg./100 cc., and culture yielded a growth of H. influenzae. Sulfadiazine was started again in doses of 2 gm. daily (approximately 0.2 gm./kg./day). When the patient did not improve, he was transferred to the Sarah Morris Hospital.

On admission to this hospital, the infant appeared to be critically ill; he was pale and lethargic and cried when disturbed. Eyes were staring, but pupils reacted to light and were equal. Head circumference was 45 cm.; anterior fontanelle was open and soft. Ear drums appeared to be normal and there was no mastoid tenderness. Neck was almost rigid. Kernig's sign was negative. Cervical lymph nodes were slightly enlarged bilaterally. Lumbar puncture yielded "ground glass" fluid under no apparent increase in pressure. There were 250 white cells, predominantly lymphocytes; glucose was 12 mg./100 cc.; total protein was 82 mg./100 cc.; chlorides were 658 mg./100 cc. This fluid yielded a pure culture of type b H. influenzae. Other laboratory findings on admission were as follows: Hgb 7.0 gm./100 cc.; RBC 3.1 million/cmm.; WBC 29.1 thousand/cmm. with 41% segmented polymorphonuclear cells, 14% nonsegmented polymorphonuclear cells, 1% eosinophils, 23% lymphocytes and 21% monocytes; ESR was 43 mm./hr. (Landau technic—normal up to 18 mm./hr.).

H. influenzae was found to be resistant to 80 u. of streptomycin, partially inhibited by both sulfadiazine and sulfathiazole and sensitive to 1.25 Oxford u./cc. pencillin G and to 0.43 u./cc. polymyxin B.

On admission to this hospital the infant was given specific rabbit anti-influenza serum 100 mg. intramuscularly. He was also given streptomycin hydrochloride 0.2 gm. intramuscularly every 4 hrs. (1.2 gm./day) and sulfadiazine 0.2 gm. orally every 4 hrs. (approximately 0.15 gm./kg./day).

On the 3rd hospital day, there was some question of the child's hearing being impaired, and he was critically ill. Nuchal rigidity was marked. Kernig's sign was questionably positive. A lumbar puncture revealed cloudy fluid under apparently normal pressure. There were 760 white cells, mostly lymphocytes; no glucose was detectable; total protein was 98 mg./100 cc.; chlorides were 658 mg./100 cc.; a relatively heavy growth of H. influenzae was obtained on culture.

Up till this time the infant's course had become progressively worse and it was not expected that he would recover. Because of this and because the infecting strain of H. influenzae was so resistant in vitro to streptomycin and penicillin yet relatively sensitive in vitro to polymyxin B (aerosporin), it was decided to try this new drug.

Streptomycin and sulfadiazine were discontinued. Polymyxin B hydrochloride 7 mg. (70,000 u.) in 1 cc. of normal saline was given intramuscularly every 4 hrs. (0.005 gm. or 50,000 u./kg./24 hrs.). The 1st day of this therapy polymyxin B 1 mg. (10,000 u. in 0.5 cc. of normal saline) was given intrathecally as well. On the 2nd day, the infant's condition appeared to be unchanged; spinal fluid was cloudy with 650 white cells, mostly lymphocytes; Pandy was 1+; glucose was 19 mg./100 cc. Culture still showed H. influenzae organisms, but they seemed fewer in number. At this time polymyxin B hydrochloride 3.5 mg. (35,000 u.) in 0.5 cc. normal saline was injected intrathecally. On the 3rd day, his condition seemed to be unimproved. Lumbar puncture revealed cloudy fluid under increased pressure; spinal fluid WBC 2.8 thousand/cmm.; culture, however, was sterile for the 1st time. At this time polymyxin B hydrochloride 3.5 mg. in 0.5 cc. normal saline was again instilled intrathecally. On the 4th day of this therapy, the infant was even more listless and toxic. On the 5th day, he was afebrile for the 1st time and though somewhat improved he still seemed lethargic, pale and dehydrated. Intravenous fluids were given, and the infant was transfused with whole blood 150 cc. On the 6th day of polymyxin therapy, the infant appeared to be markedly improved and much more alert. Lumbar puncture revealed clear fluid under no increase in pressure; spinal fluid WBC 61 (55 lymphocytes, 6 polymorphonuclear cells); total protein was 110 mg./100 cc.; glucose was 42 mg./100 cc. Culture of the spinal fluid was again sterile. He continued to be afebrile and improved rapidly. After a total of 6 days of polymyxin therapy, the drug was discontinued. His head circumference had not changed during this period. Ten days after the drug had been stopped, a lumbar puncture revealed clear fluid under apparently normal pressure; total protein was 31 mg./100 cc.; glucose was 46 mg./100 cc.; chlorides were 737 mg./100 cc. Culture was sterile. Blood Hgb at this time was 10.6 gm./100 cc.; RBC 3.46 million/cmm.; WBC 8.7 thousand/cmm. with 22% segmented polymorphonuclear cells, 12% non-segmented polymorphonuclear cells, 2% eosinophils, 58% lymphocytes, 6% monocytes. Urine was normal. There was no albuminuria at any time during the administration of polymyxin B in this case such as has been reported in some cases treated with polymyxin A.[11] The child was discharged from this hospital 18 days after admission.

Approximately 3 mos. after discharge, at 16 mos. of age, the child was re-examined. No neurologic or other physical defects were found. His urine and blood count were normal. He was able to walk a few steps without aid. A Kuhlmann test showed a mental age of 13 to 14 mos., and a Vineland social maturity test showed an age equivalent of 18 mos. The impression was that he was functioning intellectually on a low normal level for his age.*

SUMMARY

A 13 month old infant had influenzal meningitis which persisted for four weeks in spite of ordinarily adequate doses of streptomycin and sulfadiazine and the delayed administration of specific rabbit anti-influenzal serum. When the patient seemed hope-

* The author is indebted to Dr. Samuel Beck and Miss Marian Grodsky of the Department of Psychiatry, Michael Reese Hospital, for the psychologic examination.

lessly ill these medications were discontinued and a new antibiotic, polymyxin B (aerosporin), was administered. Following this, the infant recovered completely.

The infecting organism (type b H. influenzae) was resistant in vitro to 80 units of streptomycin and partially inhibited by sulfadiazine, but was sensitive to 0.43 units per cc. of polymyxin B.

Polymyxin B was given both intramuscularly and intrathecally. On the fourth day of this new therapy, the child seemed to be more toxic, but improvement thereafter was rapid, and there were no other symptoms or signs of toxicity which might be attributed to the polymyxin. Re-examination of this infant approximately three months later revealed that he was functioning intellectually on a low normal level for his age. There were no neurologic or other physical defects.

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Spanish Abstract

Meningitis Influenzal, Restablecimiento de un Caso de Cuatro Semanas de Duración con el Uso de una Nueva Droga

Un infante de 13 meses de edad tenía meningitis influenzal que persistió por 4 semanas a pesar de dosis ordinariamente adecuadas de estreptomicina y sulfadiazina y la tardada administración del suero anti-influenzal de conejo específico. Cuando el paciente se vió desesperadamente enfermo se le descontinuaron estas medicaciones y se le administró un nuevo antibiótico, polimixina B (aerosporin). Después de esto el infante se restableció completamente.

El organismo infectante (tipo b H. influenzae) era resistente en vitro a 80 unidades de estreptomicina y parcialmente inhibido por la sulfadiazina; pero fué sensible a 0.43 unidades por cc. de polimixina B.

La polimixina B fué administrada intramuscularmente e intratecalmente. Al cuarto día de esta nueva terapia, el niño pareció estar más tóxico; pero su mejoría después de eso fué rápida, y no hubieron otros signos o síntomas de toxicidad que puedan ser atribuídos a la polimixina. Al reexaminar a este infante aproximadamente tres meses más tarde, se encontró que estaba funcionando intelectualmente a un nivel más bajo del normal para su edad. No hubieron otros defectos físicos ni neurológicos.

29th Street and Ellis Avenue

PULMONARY TUBERCULOSIS IN CHILDREN TREATED WITH STREPTOMYCIN

By EUGENE T. MCENERY, M.D., HENRY C. SWEANY, M.D., AND GEORGE C. TURNER, M.D.
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THE use of streptomycin in the treatment of tuberculosis has been reported extensively[1-5] since the early work of Waksman[1] and Feldman and Hinshaw.[2] Alterations in the course of tuberculous infection observed by them were unprecedented. The reports on its use in children have been limited largely to cases of meningitis and miliary tuberculosis, although Sanford[3] has reported four cases of pulmonary tuberculosis, treated with good results. The majority of reports in the literature are those dealing with adult tuberculosis. The authors of this study have felt that a larger series of cases in children should be reported.

The opportunity for observing a large group of children with tuberculosis over a 15 year period occurred. A report of the clinical experience as recorded in this series of cases is now made.

The general plan of treatment during the 15 years before the use of streptomycin was rest in bed, good nursing care and nutritious diet. Many primary lesions of tuberculosis in children, after a long and tedious course of such treatment, may reach a stage where the tuberculosis process can be arrested. However, some of the patients treated did not get better. A disseminated pulmonary tuberculosis developed and the patient died. There was no way to foretell when a case would recover or would progress to a fatal outcome.

The results in the treatment of tuberculosis in adults with streptomycin had been encouraging so it was decided in the fall of 1947 to use the treatment for all suitable patients in the sanitarium.

PLAN OF STUDY

All cases were under observation for periods of from 2 to 36 mos. All had positive examinations for tubercle bacilli from either sputums, gastric washings or bronchial secretions. The positive sputums were confirmed with cultures and guinea pig inoculations. The patients all had positive Mantoux tests. Roentgenograms all showed lung infiltration of varying degree. A complete history with special emphasis on contact with a person with tuberculosis was taken on each child. All the criteria for a diagnosis of an active pulmonary process were present before any streptomycin therapy was started. Each child's history was reviewed by a "Streptomycin Board" consisting of 3 clinicians, 1 thoracic surgeon and 1 pathologist. Its function was to evaluate each case and suggest a plan of streptomycin therapy. The Board also suggested when the record should be returned for review and evaluation. Ten cases were rejected by the Board because they were not considered suitable. These children had progressed satisfactorily under conservative treatment and it was felt that streptomycin therapy would add nothing to their progress.

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TABLE I

CASES OF TUBERCULOSIS TREATED WITH STREPTOMYCIN

	Race and Sex	Age	Type	Wt. Before Drug	Wt. 3 mos.	Wt. 6 mos.	Wt. 10/48	Daily Dosage	Days	Total Dosage
CB	N-M	8 mos.	PP	6.4 kg.	7.7 kg.	10.0 kg	10.9 kg.	0.1 gm.	120	17 gm.
DM	W-M	10 mos.	PP	6.4	7.7	8.6	9.5	0.1 gm.	120	17 gm.
SB	W-M	12 mos.	PP	8.6	9.5	10.0	10.4	0.5 gm.	120	60 gm.
MP	W-F	18 mos.	PP	9.1	10.4	11.3	12.7	0.3 gm.	60	18 gm.
RR	N-F	2 yrs.	PP	10.9	13.6	15.4	16.3	0.25 gm.	120	60 gm.
KJ	W-F	2 yrs.	PP	13.2	13.6	14.1	15.0	0.3 gm.	120	38 gm.
MG	N-M	2½ yrs.	PP	14.5	15.4	15.9	16.8	0.4 gm.	60	24 gm.
WB	W-M	3 yrs.	PP	10.4	10.9	12.7	14.1	0.5 gm.	120	60 gm.
KM	W-F	3 yrs.	PP	14.5	14.5	15.0	15.9	0.5 gm.	100	50 gm.
SC	N-M	3½ yrs.	PP	13.2	14.1	14.5	15.0	0.5 gm.	120	60 gm.
MW	N-M	4 yrs.	PP	19.1	19.5	20.4	21.8	0.5 gm.	150	75 gm.
LD	N-F	5 yrs.	PP	18.6	20.9	23.1	24.5	0.5 gm.	120	60 gm.
EC	N-F	5 yrs.	PP	18.1	19.5	19.1	20.0	0.2 gm.	120	24 gm.
DM	N-F	7 yrs.	PP	21.8	23.6	25.4	26.3	0.5 gm.	120	60 gm.
JH	N-F	7 yrs.	PP	18.1	19.1	20.4	20.9	0.5 gm.	120	60 gm.
VW	N-F	11 yrs.	FA	32.7	34.9	36.3	31.8	0.5 gm.	122	61 gm.
AW	N-M	12 yrs.	FA	46.7	49.4	51.7	51.7	0.5 gm.	120	60 gm.
DP	N-F	12 yrs.	PP	39.9	39.5	42.6	44.5	0.5 gm.	120	60 gm.
PR	N-M	13 yrs.	PP	35.8	40.8	43.1	46.3	0.5 gm.	120	60 gm.
GJ	N-F	13 yrs.	PP	43.1	47.6	47.6	52.1	0.5 gm.	120	60 gm.
CW	N-F	13 yrs.	FA	39.9	40.8	46.3	47.2	0.5 gm.	120	60 gm.

Each case was closely observed clinically during the course of treatment. Roentgenograms were taken once a month during active use of the drug and every 2 to 3 mos. after stopping streptomycin treatment. All patients were kept on essentially the same rest program. Blood counts and sedimentation rates were taken at least once a month. After streptomycin therapy was stopped, stained smears of gastric washings and bronchial secretions and cultures were made. Two negative examinations of gastric washings and 1 negative examination of a bronchial secretion were required before a child could be discharged.

Types of Tuberculosis

Eighteen of the 21 cases were classified as having a progressive primary lesion. This type of lesion is of relatively recent origin, sometimes demonstrated on physical examination by impaired percussion resonance and suppressed breath sounds, but more than likely not revealing any change in physical signs. Roentgenograms show a soft infiltrative process usually extending out from the hilum to the periphery of the lung, with some enlargement of hilar shadows. Three cases were classified as far-advanced adult type of pulmonary tuberculosis, with activity and large cavities. These children had failed to respond to bed rest and pneumothorax regime and had been on a downward course for a period of 2 yrs.

The ages (see Table I) varied from 8 mos. to 11 yrs. for the patients with progressive primary lesions, while those with adult type were 11, 12 and 13 yrs. respectively. Fifteen were Negro and 6 white, 9 were male and 13 female.

Dosage.—The majority of the cases received streptomycin 0.5 gm. in divided doses, twice daily, in the beginning of this study. This has been decreased now to 0.3 gm. once daily.

Duration of treatment.—The majority of cases were placed on dosage of drug for 120 days. This has been reduced now to 90 days.

Blood levels.—These have not been taken as a routine measure, but spot checking on cases has shown blood levels in the morning before injection to vary from 0.5 to 1.0 μgm./cc. Six hours after administration of streptomycin 0.3 gm., the blood level had risen to 6.0 to 8.0 μgm./cc. of blood, a good therapeutic level.

Toxic manifestations.—Using a smaller dosage, 0.5 gm., once daily, toxic reactions have not been present. No auditory or vestibular disturbance has been noted during active therapy or after the drug was stopped. Audiometer and caloric tests were not done. Simple clinical tests for hearing and equilibrium were found to be normal. Skin reactions have not been present although 1 patient who had been receiving streptomycin 2.0 gm. daily for 10 days previous to admission to the hospital had a diffuse erythematous rash all over his body which persisted for 5 days after the drug was stopped. He was started on 0.1 gm. daily after the rash disappeared and no further trouble was experienced.

Urinary Findings.—A trace of albumin has persisted in about 65% of these cases while under active drug therapy, but this has disappeared when the drug was stopped. It was believed that this was due to a transient irritation of the kidney.

Clinical Response.—The response has been the same in all cases. This has occurred in 7 to 10 days. The following reactions have been noted consistently: a drop in temperature, improvement in appetite, change in disposition and lessened irritability. Expectoration is a negligible symptom before or after treatment in this type of case. The psychologic factor, which influences the above observations in treating adults, played no role in the treatment of these children. No injurious effect could be observed, except in the case of the child who received 2.0 gm. of the drug daily for 10 days before admission and developed a generalized rash.

Physical Findings.—In the progressive primary cases, even though the general well-being of the patient improved in the short period of 7 to 10 days, it was at least 1 mo. before any changes were noted in the physical examination; then improved percussion resonances, better transmission of breath sounds and fewer rales were noted.

The physical findings remained about the same in the adult type, and became more marked in 2 cases. One child became decidedly worse and died 7 mos. after streptomycin therapy had been completed.

Roentgenograms.—The changes in the monthly films were slow to make their appearance. It was usually 3 mos. before a definite change could be noted. Improvement has continued 8 mos. after stopping the drug.

Case Histories

Case 1 (Figs. 1 and 2).—S.B., a white male infant 9 mos. of age. Contact: Step-brother, 18 yrs. old, an ex-veteran who died of pulmonary tuberculosis when the child was 7 mos. old. Five mos. before admission to hospital, had developed a cold; gastric washing positive for tubercle bacillus. Physical examination showed a fairly well nourished baby with impaired resonance and fine crepitant rales at the right base. Three mos. after admission the pulmonary findings changed; there were rales present on both sides of the chest, daily temperature of 38.3° to 39.4° C. Patient was started on penicillin because it was thought he had pneumonia; condition did not improve on this drug and the treatment was changed to streptomycin. RBC count 5.38 million/cmm.; WBC count 12 thousand/cmm.; ESR 15 mm./hr. Patient's condition improved and he became less toxic during the 1st wk. of therapy. Roentgenogram showed gradual improvement. Three mos. after streptomycin was started again, ESR was 6 mm./hr. and again 1 mo. later 2 mm. He was discharged 13 mos. after admission, with cultures on gastric washings and bronchial secretions negative. Since leaving the hospital he has gained 2.3 kg. and is doing well.

Case 2 (Figs. 3 and 4).—K. J., a white female, aged 2 yrs., contact unknown. Two mos. after admission to the Children's Memorial Hospital, she developed fever with slight cough, loss of appetite, irritability and easy fatigue. Roentgenograms revealed an exudative lesion at the right base. Gastric washing positive for tubercle bacilli. Admitted to Municipal Tuberculosis Sanitarium 3 mos. later and started on streptomycin treatment. RBC count 4.69 million/cmm.; WBC count 7.5 thousand/cmm.; ESR 15 mm./hr. Roentgenogram showed gradual clearing of progress at right base. Physical findings have improved, transmission of breath sounds normal and no rales present. Cultures on gastric washings negative for tubercle bacilli. Four mos. after streptomycin was started, ESR was 8 mm./hr. and again 2 mos. later, 2 mm./hr.

Case 3 (Figs. 5 and 6).—C.B., a Negro male infant, aged 7 mos., contact unknown. Developed a cold and was admitted to Cook County Hospital. Gastric washing positive for tubercle bacillus. Admitted to Municipal Tuberculosis Sanitarium 4 mos. later. Physical examination revealed a poorly nourished infant with impaired percussion resonance at the right apex with rales and amphoric breathing. General condition poor. Started on streptomycin therapy; RBC count was 3.5 million/cmm., WBC count 10 thousand/cmm., ESR 20 mm./hr. General condition improved in 1 wk. His appetite increased, he was less toxic. Roentgenogram showed gradual improvement. Three mos. after streptomycin was started ESR was 14 mm./hr, again 4 mos. later 10 mm., and 6 mos. later 8 mm. Sputum is now negative for tubercle bacillus and he is awaiting discharge from hospital.

Case 4 (Figs. 7 and 8).—W.B., white male aged 3½ yrs., contact unknown. Developed rubeola with a cough which lingered after rash disappeared. In 2 mos. taken to Children's Memorial Hospital where physical examination showed emaciation, large bilateral cervical lymph nodes, impaired percussion resonance at both right and left apices with rales and amphoric breathing. Gastric washings were positive for tubercle bacilli. Child was started on streptomycin 2 gm. daily in divided doses of 0.5 gm. 4 times daily. After 10 days, he was transferred to the Municipal Tuberculosis Sanitarium. On admission, he was toxic and a diffuse erythematous rash covered his whole body. The pulmonary findings had not changed. He was given intravenous fluids and blood transfusions, and because of the rash the streptomycin was stopped. RBC count was 3.7 million/cmm.; WBC count 8.5 thousand/cmm.; ESR 29 mm./hr. After 5 days, the rash faded and he was started again on streptomycin 0.1 gm. once daily. In 2 wks., his temperature returned to normal, and he began to improve. Physical findings changed slowly and the roentgenogram showed there was a gradual improvement. Three mos. later ESR was 15 mm./hr., again in 2 mos. 17 mm., and in 6 mos. 8 mm. His sputum is still positive for tubercle bacillus. He is still under observation.

Case 5 (Figs. 9 and 10).—C.W., aged 13 yrs., Negro female; contact, father. Child admitted to the Municipal Tuberculosis Sanitarium with a far-advanced, adult type of pulmonary tuberculosis. Positive sputum. RBC count was 4.27 million/cmm.; WBC count 8.7 thousand/cmm.; ESR 25 mm./hr. Pneumothorax was established on left side and maintained for 1 yr. Pneumoperitoneum for 6 mos. Continued bed rest. All these measures failed to check the slow progress of the disease. Two and a half yrs. after admission she was started on streptomycin 0.5 gm. daily. Physical findings did not improve. Rales became more numerous and cavity enlarged. Roentgenograms showed extension of the process. Five mos. later ESR was 20 mm./hr., again 7 mos. later 15 mm. Sputum remained positive.

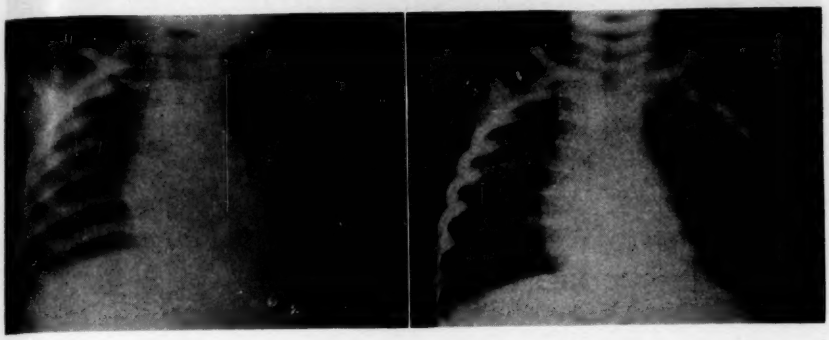

FIG. 1 (left). S. B., before streptomycin therapy. Progressive primary type.
FIG. 2 (right). S. B., 8 mos. after treatment.

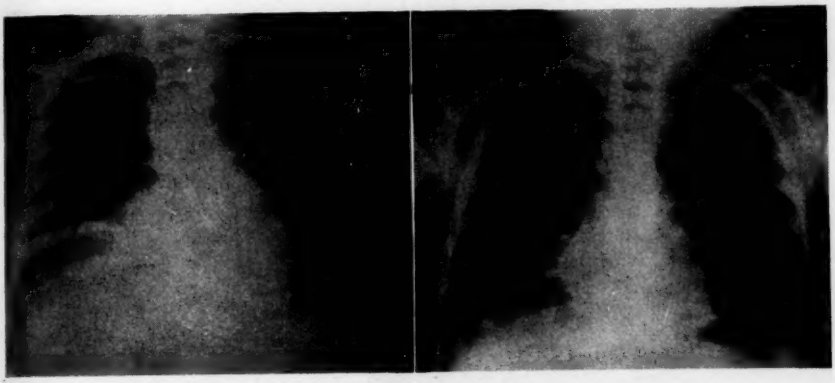

FIG. 3 (left). K. J., before streptomycin therapy. Progressive primary type.
FIG. 4 (right). K. J., 7 mos. after treatment.

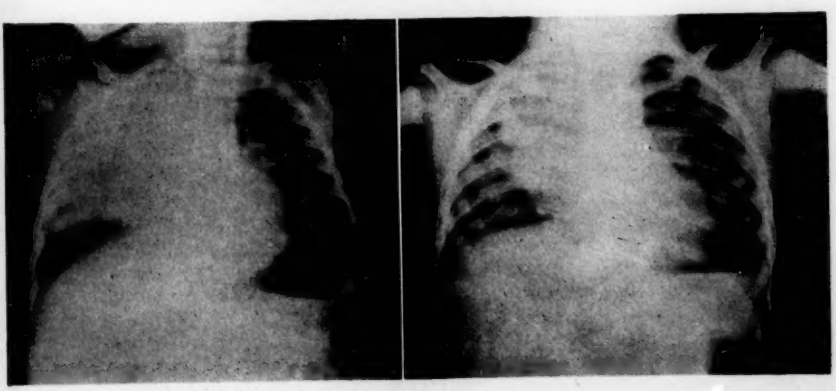

FIG. 5 (left). C. B., before streptomycin therapy. Progressive primary type.
FIG. 6 (right). C. B., 8 mos. after treatment.

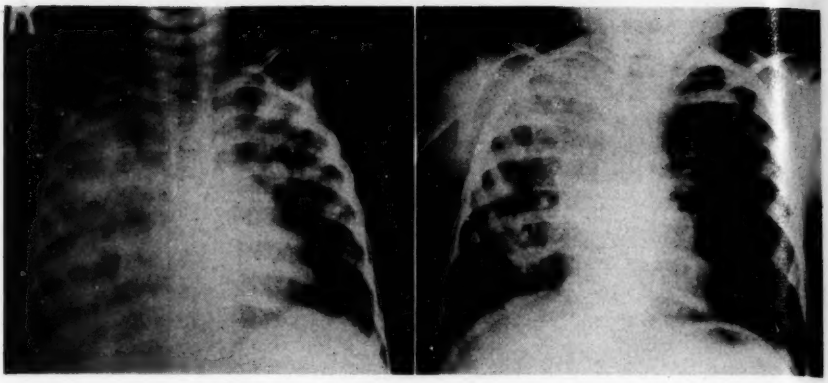

FIG. 7 (left). W. B., before streptomycin therapy. Progressive primary type.
FIG. 8 (right). W. B., 8 mos. after treatment.

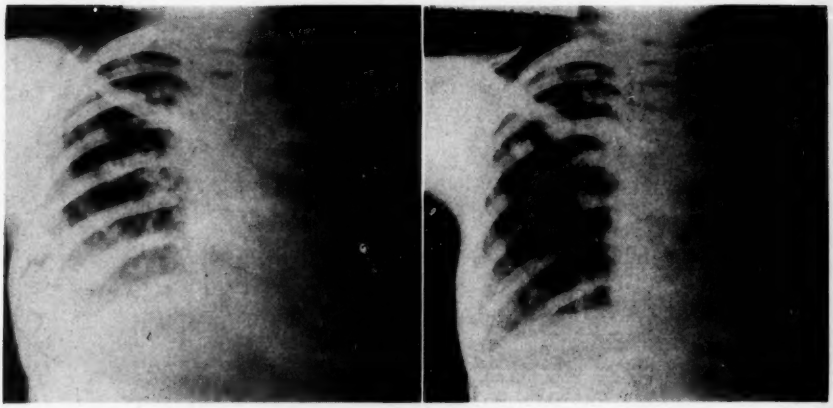

FIG. 9 (left). C. W., before streptomycin therapy. Adult type with cavities.
FIG. 10 (right). C. W. Lesions have progressed.

FIG. 11 (left). V. W., before streptomycin therapy. Adult type with cavities.
FIG. 12 (right). V. W., 11 mos. after treatment. Lesion more extensive, numerous cavities.

Patient's condition became increasingly worse and she died after 120 days of streptomycin therapy. Streptomycin therapy had only a transient effect on this patient.

Case 6 (Figs. 11 and 12).—V.W., aged 12 yrs., Negro female, contact unknown. Developed a cough and felt tired. She was admitted to the Municipal Tuberculosis Sanitarium Dispensary where sputum was found positive for tubercle bacilli. Physical examination revealed a thin, toxic girl with cavities at both right apex and left base. RBC count was 4.22 million/cmm.; WBC count 6.65 thousand/cmm.; ESR 19 mm./hr. Nine mos. later, ESR was 22 mm./hr.; again 8 mos. later, 26 mm. Bed rest for 3 mos. did not change the progress of the disease. She was started on streptomycin therapy 4 mos. after admission. Her general well-being improved, she was less toxic, her appetite improved and she gained in weight. Physical findings did not improve. Rales increased and the cavities enlarged. Roentgenograms showed changes for the worse. Her condition became worse, apparently only temporarily affected by streptomycin therapy. She is now in a critical condition.

Discussion

Many of the children with progressive primary lesions have been discharged from the hospital. These have been followed closely at monthly intervals. A few of them, previous to streptomycin therapy, had been confined to the hospital for a period of two years because of repeated positive sputum for tubercle bacilli. One child, in addition to his pulmonary lesion, had tuberculosis of the elbow joint with a discharging sinus. This had been operated on, and casts had been on and off for two years. Two weeks after streptomycin therapy was started the sinus closed and has remained closed after one year.

Experience with this series of cases indicates children may be treated successfully with streptomycin and the duration of their hospital admission shortened. The sputum has become negative for tubercle bacilli in all but 4 of the 21 patients. The criteria for discharge from the sanitarium were two consecutive gastric washings and one bronchial secretion, negative for tubercle bacilli on smear and culture. Two of cases with positive sputum have the adult type and two the progressive primary type of tuberculosis. The tubercle bacilli from these four cases have shown slight resistance to streptomycin on sensitivity tests.

The dosage of the drug used in the cases has been low and it is believed that this is the reason that no toxic reactions have been observed. Even though the dosage has been low a good clinical response to the drug has been demonstrated. Single daily doses have lessened the occurrence of subcutaneous nodules. At times these caused a great deal of discomfort to the children.

The authors believe that children with primary tuberculous lesions are not necessarily suitable for treatment with streptomycin. If the case has been under observation for a time long enough to observe that the lesion is not progressing satisfactorily under conservative treatment, then streptomycin should be used. This form of treatment does something to the tuberculous lesion which we have never seen before. There is an immediate improvement in the clinical well-being of the child. He is less irritable, the temperature drops to normal, the appetite improves and he gains in weight. The physcial findings are slow to improve, at the earliest two months, and the changes in the roentgenograms may take three months. Streptomycin is a drug which should be added to the armamentarium of treating primary tuberculous lesions.

On the basis of clinical, roentgenologic and bacteriologic observations, it was demonstrated in this series of 21 cases that the degree of therapeutic efficiency of streptomycin is definitely related to the type and stage of the pulmonary lesion. Improvement occurred much more frequently in patients with early and acute disease processes than with those having late and chronic lesions.

Conclusions

The use of streptomycin in the treatment of primary progressive tuberculosis has uniformly lessened and in most cases obliterated the toxic manifestations of the disease, and has reversed the general downward clinical course of the disease in a series of 21 cases. The physical findings improved and decreased roentgenologic changes followed the clinical and physical improvement. Conversion of sputum from positive to negative findings was completed in four to five months in 89% of primary progressive lesions.

The group of three cases with the adult type of pulmonary tuberculosis was too small to be statistically significant, but from observations of these children it is believed that the results were similar to cases of chronic pulmonary tuberculosis in adults treated with streptomycin in this and other institutions. Two of these cases were only temporarily improved. One of these died and the other is now in a terminal stage. The third child is awaiting surgery.

Streptomycin therapy should not be considered a cure-all; its use is still in the experimental stage and a larger number of cases will have to be observed over a longer period of time.

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Spanish Abstract

Tuberculosis Pulmonar en Ninos Tratada con Estreptomicina

Se reportan veintiún caso de tuberculosis pulmonar en niños. Dieciocho tenían lesiones primarias progresivas y tres tuberculosis pulmonar tipo adulto.

Las edades de los pacientes variaron de 8 meses a 13 años. Todos tuvieron análisis positivos de tuberculina; lavados gástricos y las secreciones bronquiales fueron positivas para el baccilo tubérculo. La observación había sido por dos meses a tres años antes de principiar con la terapia de estreptomicina.

Todos los pacientes tuvieron la misma respuesta clínica: la temperatura volvió a normal, las manifestaciones tóxicas se redujeron, el apetito y bienestar mejoraron en una semana. Los descubrimientos físicos mostraron poco o casi ningún cambio por dos meses y los descubrimientos de roentgenograma fueron aún más lentos, habiendo pasado tres meses antes de que se notara un aclaramiento.

La dosis de estreptomicina fué la misma para todos los niños, 3 gm. una vez al día. Duración del tratamiento: 18 casos 120 días, los otros 60 días.

No se desarrollaron síntomas tóxicos usando dosis pequeñas y la respuesta clínica fué satisfactoria. Todos menos cuatro de los casos tuvieron conversión de esputo, dos en el tipo primario progresivo y dos en el tipo adulto. Una muerte ocurrió en el tipo adulto. Todos los resultados favorables ocurrieron en el tipo más reciente de lesión. El tipo adulto mejoró clinicamente; pero esto fué solamente por una corta duración. La droga dejó de interponerse al progreso de este tipo de lesión ya en los descubrimientos físicos o en el exámen roentgenográfico.

La estreptomicina es una droga de valor, pero está todavía en la etapa de experimentación y en grandes series de casos se tendrá que observar por un período largo de tiempo.

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ACUTE PULMONARY ASPERGILLOSIS

Report of a Case

By A. J. HERTZOG, M.D., T. S. SMITH, M.D., AND M. GOBLIN, M.S.
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PULMONARY aspergillosis has been recognized for over a hundred years. Hughes Bennet is given credit for reporting the first case in 1842.[1] The following two cases are of particular interest because of the occurrence in siblings and the rapidly fatal course. The younger child is the first case of pulmonary aspergillosis in a series of 55,000 autopsies at the Department of Pathology of the University of Minnesota.

CASE REPORT

R. B. was a white male, 5 yrs. of age, admitted to the pediatric service of the hospital. Good health had been enjoyed until approximately 1 mo. prior to his death, when he developed an acute respiratory infection of a few days' duration. He developed a low grade fever and rapid respiration. He had been hospitalized elsewhere 5 days previously when his temperature was found to be 40.2°C. and chest roentgenograms revealed bilateral infiltration. The clinical diagnosis at that time was bronchopneumonia. Although he received penicillin 100,000 u. every 3 hrs. daily, temperature remained between 39.4° and 40°. Showing no change, he was sent to this hospital for further study and treatment. On admission, he was acutely ill with cyanosis of the lips and nailbeds. Temperature was 39.2° and respiration 84/min. Tongue was heavily coated. There was minimal cervical lymphadenopathy. Chest was resonant throughout with symmetric rapid costal breathing and a few crepitant rales over the right lower lobe. Liver was palpable 3 cm. below the costal margin. The remaining part of the examination showed nothing of note. Diffuse bilateral pulmonary infiltration, thought to be consistent with pulmonary tuberculosis, was present on the chest roentgenograms (Fig. 1). Hgb. was 10.8 gm./100 cc.; leukocyte count was 30.8 thousand with 64% neutrophils, 29% lymphocytes and 1% eosinophils. Cultures from the throat showed no growth of fungus. Cultures of the blood, spinal fluid and aspirated lung material showed no growth of bacteria or fungi. Spinal fluid examination revealed 18 cells/cmm. fluid with 11% neutrophils and 89% mononuclears. Chemotherapy consisted of penicillin 100,000 u., streptomycin 0.5 gm. and sulfadiazine 0.5 gm. every 6 hrs. In spite of chemotherapy and oxygen, there was no improvement. He remained cyanotic and died 20 hrs. after admission to the hospital.

AUTOPSY

Postmortem examination was made 5 hrs. after death. The body was that of a well nourished, well developed child with cyanosis of the lips and fingers. Pleural, pericardial and peritoneal cavities all appeared normal. Lungs, which were heavy, large and pinkish-gray in color, were removed intact. Small, flat, grayish-white areas studded the surfaces, which on palpation appeared indurated. Both lungs showed generalized consolidation with marked decrease in crepitation. On section, after fixation in formalin, discrete and confluent grayish-white nodules were seen scattered diffusely throughout all lobes of both lungs. These nodules measured up to 2 cm. in size (Fig. 2). Hilar lymph nodes were enlarged and soft. Liver weighed 650 gm. and each kidney, 75 gm. Both organs revealed some cloudy swelling. Heart weighed 125 gm.; spleen, 50 gm.; both were apparently normal. Brain had no remarkable findings. Nodules seen in the lungs were not noted on gross examination in any of the other organs.

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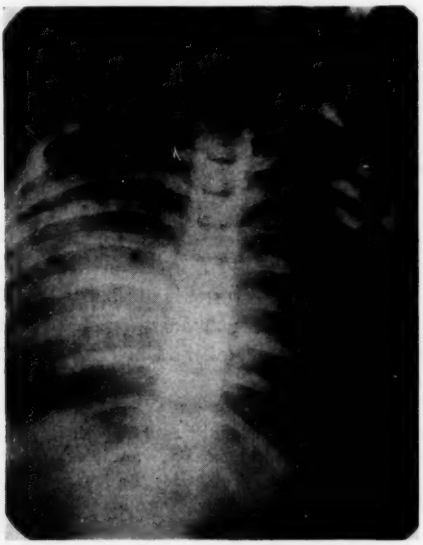

FIG. 1. Chest roentgenogram of R. B. showing diffuse pulmonary infiltration.

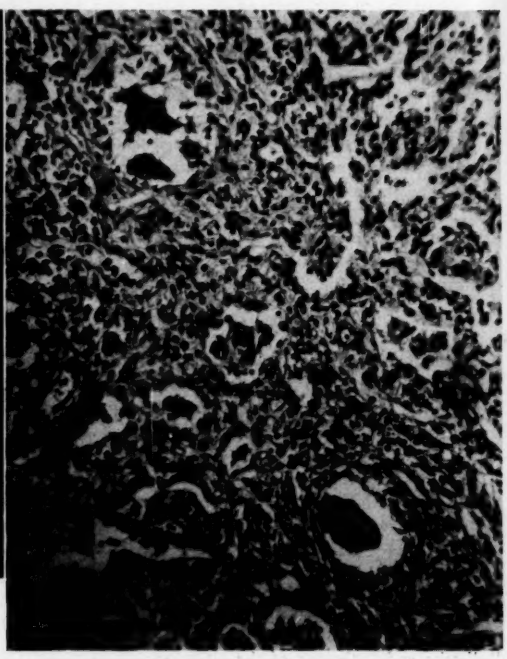

FIG. 2 (left). Cut section of lung showing diffuse nodularity.
FIG. 3 (right). Microscopic section of lung showing granulomatous inflammatory reaction with giant cells.

Microscopic examination of the lungs demonstrated a widespread patchy granulomatous inflammatory process with tubercles present. Tubercles were composed of a center of neutrophils and a peripheral zone of epithelioid cells and large multinucleated giant cells (Fig. 3). Most of the alveoli between the tubercles were filled by large numbers of neutrophils, lymphocytes and mononuclear cells. Bronchi contained a fibrinopurulent exudate. Liver cord cells were pale and granular. Hilar lymph nodes were large and hyperplastic with prominent lymph follicles. Meninges of the brain appeared normal. Capillaries in the cortex were congested but the gray and white matter was normal. Follicles of the spleen were prominent and the pulp sinuses contained a few plasma cells. Adrenals, kidneys and cardiac myocardium all appeared normal. Granulomas or tubercles were not seen microscopically in any tissues other than the lungs.

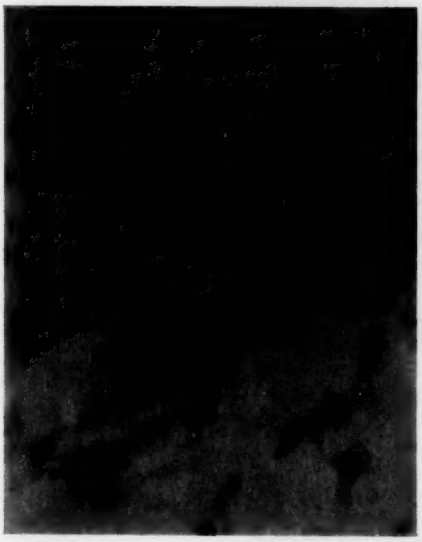

FIG. 4. Microscopic section of lung under oil immersion showing hypha of aspergillus as seen by Gram stain.

BACTERIOLOGIC STUDIES

Gram stains of paraffin sections of the lung tissue showed the presence of numerous large hyphae and scattered spores (Fig. 4). Acid fast organisms were not demonstrated. Direct examination of fresh lung tissue revealed no acid fast bacilli or other bacterial organisms, but a few septate fungal hyphae were present. Bacteriologic cultures from Northwestern Hospital and the Minnesota Department of Health on several types of media (Brewers', blood agar, blood cystein dextrose, Sabouroud, Clawson's broth and plain agar) produced a profuse growth of a green aspergillus in 48 hrs. Subsequent cultures of the culture media and of the saline, sand and other materials used in preparing the tissue suspension produced no growth. Subcultures of the aspergillus were reported to be Aspergillus fumigatus Fres. Guinea pigs injected subcutaneously revealed no evidence of bacterial infection after 6 wks.

Coincident with R. B.'s illness, his sister, F. B., a white female aged 7 yrs., also became ill with fever and rapid respiration. Temperature was 37.4° C.; pulse, 160/min.; respiration 104/min. As she appeared extremely toxic, she was given penicillin 300,000 u. in oil and admitted to the same hospital on the same day. Chest roentgenogram (Fig. 5) was similar to that of her brother, showing bilateral pulmonary infiltration and interpreted as bronchopneumonia. She was given penicillin, streptomycin, sulfonamides and whole blood. There was no improvement and she died 5 days later at that hospital, just 2 days prior to her younger brother. Postmortem examination was not done.

Father, mother and 11 yr. old brother are all living and well. The whole family except for the 5 yr. old boy had 70 mm. chest films about 1 yr. previously, during a routine tuberculosis survey. These were interpreted as normal. However, a review of these films at this time showed an infiltration at the apex of the right lung of the 7 yr. old girl. Standard roentgenograms of the father, mother and older brother were then taken and are reported as negative. The family lives on a farm near Melrose, in Stearn County, Minnesota. The two youngest have been there all their lives.

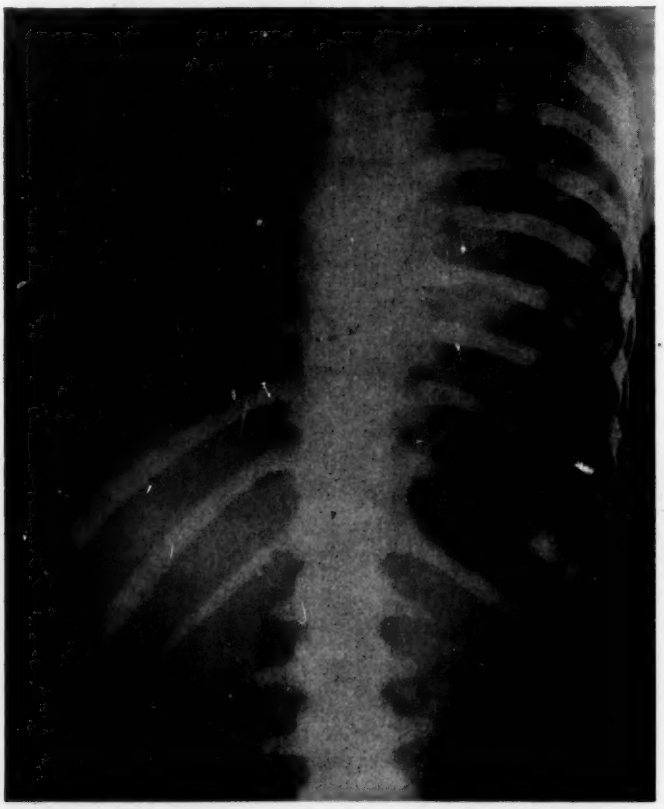

FIG. 5. Chest film of F. B. showing diffuse pulmonary infiltration.

DISCUSSION

The diagnosis of acute pulmonary aspergillosis seems firmly established in the first case based upon anatomic and bacteriologic findings at autopsy. The clinical course and the chest roentgenograms were so similar in the two siblings that it is believed that the two children died of the same disease. The fact that the routine 70 mm. roentgenograms had an infiltration in the right apex of the 7 year old girl raised the question of a latent infection in this child.

The mold Aspergillus is widely distributed in soil, cereals, unmilled grain, hay, animal dandruff, dust about poultry pens, and in such birds as pigeons and parrots. Of the many strains of aspergillus present, only the Aspergillus fumigatus and Aspergillus niger have

been proved to be pathogenic for man.[2] It has been considered an occupational hazard among pigeon stuffers who are in the habit of feeding the birds with their mouths. Coe[3] reports a case of pulmonary aspergillosis in a stockyard worker who was in constant contact with livestock, animal feed and contaminated dust. These children living on a farm would have ample opportunity to come in contact with the aspergillus fungus in the same manner. The rarity of the disease in man in view of the widespread distribution of the fungus shows that either most strains of the fungus are nonpathogenic or that man is relatively immune. Therefore, clinical infection apparently rests upon massive or repeated doses of a pathogenic strain or a lowered tissue resistance secondary to a concomitant pulmonary infection.

Aspergillus has a special affinity for the respiratory tract of man and animals. The organism may be a primary or a secondary invader. The infection may be limited to bronchi or extend diffusely into the pulmonary alveolar tissues. The disease may be either acute or chronic in its course. The usual history is the chronic productive cough, pleurisy, weakness, anorexia and weight loss.[4] The roentgenographic findings are similar to those of chronic pulmonary tuberculosis. Sputum examination is negative for acid fast bacilli, but positive for the fungus. Acute fulminating aspergillar pneumonia as shown in these two cases is unusual. The roentgenographic findings of aspergillosis are difficult to distinguish from the findings of miliary tuberculosis. Doub[5] reported a family of five consisting of a mother and four children who had diffuse miliary lesions throughout both lungs, which later went on to complete calcification. Aspergillus was cultured from the sputum of these five cases. There is no characteristic blood picture, but some cases show an eosinophilia up to 10%.[1-4,6] The final diagnosis is usually made upon identifying the fungus from sputum or postmortem examination of the lungs. Potassium iodide has been the only drug used with any beneficial results. Penicillin, streptomycin, sulfonamides, desensitization, neoarsphenamine, bismuth and many other agents have been tried without success.

Summary

Two fatal cases of acute pulmonary aspergillosis in siblings aged five and seven years are reported. The details of an autopsy in one case are recorded. The fungus in this case proved to be Aspergillus fumigatus Fres.

Acknowledgment

Acknowledgment is made to Dr. L. B. Kuhlman of Melrose, Minn., and Drs. E. Platou, R. Tudor and A. Hill of Minneapolis, Minn., for permission to report these cases. The authors also wish to express appreciation to Dr. K. B. Raper of Peoria, Ill., for species identification.

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SPANISH ABSTRACT

Aspergilosis Pulmonar Aguda Relato de un Caso

La aspergilosis pulmonar es secundaria al Aspergillus fumigatus o Aspergillus niger, el cual se puede encontrar en el suelo, cereales, grano sin moler, heno, caspa animal, polvo en lugares donde hay aves de corral y pájaros, tales como palomas y papagayos. El hongo tiene una afinidad especial por las vías respiratorias, produciendo una enfermedad granulomatosa similar a la tuberculosis. Los síntomas generales son una tos productiva crónica, pleuresía, debilidad, anorexia y pérdida de peso. Rara vez la enfermedad está fulminante con fiebre, anorexia, dispnea, cianosis y muerte en un período de días como se describe en los informes de casos. La diagnosis final se hace generalmente identificando el hongo en el cultivo del esputo o después de la muerte. Los casos crónicos pueden calmarse con la formación de tubérculos cálcicos y los casos agudos son siempre fatales. Hasta la fecha no se conoce ningún tratamiento digno de mención.

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INFLUENZAL VACCINATION IN INFANTS AND CHILDREN

By M. G. PETERMAN, M.D., AND V. KORES, M.D.
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IT HAS been demonstrated conclusively in recent years that subcutaneous injection of influenzal virus vaccine will produce an immune response in most adults.[1,2] It has been shown also that this response, which consists of an increase in serum antibody titer, is directly related to immunity to clinical influenza.[3-9]

Francis and Magill[10] and Rickard and Horsfall[11] have found that the serum of the newborn infant has about the same antibody titer as that of its mother, but that after the first month of life there is a marked drop in titer which lasts from the 12th to 18th month when it begins to rise, reaching the maximum in the 20 to 40 year age group. Children, especially those under the age of five years, need the protection which immunization may offer.

Relatively little is known about the response of infants and children to the injection of influenzal vaccine. Cohen and Schneck[12] have reported recently data on the subcutaneous injection of the vaccine in 100 children and found that those under two years of age did not develop any increase in antibody titer, whereas the response was present in the 2 to 13 year old group.

Tuft[13] recognized the value of the skin as an immunologic organ and demonstrated that adequate immunity could be produced against typhoid fever by the intracutaneous injection of small amounts of typhoid vaccine. Later, satisfactory immune responses were obtained by the intracutaneous injection of diphtheria toxoid[14-16] and scarlet fever toxin.[17-19] Van Gelder et al.[20] reported results obtained by both the intracutaneous and the subcutaneous injection of influenzal vaccine. They found that one injection of 0.1 ml. of vaccine injected intracutaneously produced a higher serum antibody titer than 1.0 ml. subcutaneously or two intracutaneous injections at one week intervals. Because of these results, it was decided to investigate the response by children to the intracutaneous injection of influenzal vaccine.

METHODS AND MATERIALS

From Nov. 1947 to Feb. 1948, 49 children ranging in age from 4 mos. to 13 yrs. were given 0.1 ml. each of influenzal virus vaccine, types A and B,* intracutaneously. Blood for serum antibody titer determination was drawn at the time of vaccination and again 4 wks. later. Four wks. was chosen as the interval for the determination of titers as it has been demonstrated that the immune response is probably the greatest at that time. Antibody levels were determined by a modification of the method described by Hirst.†[21,22] Each child's temperature was taken every 4 hrs. for 24 hrs. following vaccination, or longer if the temperature was elevated.

RESULTS

Table I is a summary of the pre- and postvaccination titers together with the fold increase. As all of the antibody titers were not done on the same day with the same lot of antigens, the titers on the

From the Milwaukee County Hospital Department of Pediatrics and the Home for Dependent Children, Milwaukee, Wis.

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* Furnished by Eli Lilly, Co., Indianapolis, Ind., in September 1947.

† Titers were determined by Dr. H. M. Powell of the Eli Lilly Co.

TABLE I

RESULTS OF SERUM ANTIBODY TITER DETERMINATIONS TOGETHER WITH FOLD INCREASE IN TITER AFTER INTRACUTANEOUS INJECTION OF INFLUENZAL VACCINE

Name	Age	Prevaccination Titer		Postvaccination Titer		Fold Increase	
		Type A	Type B	Type A	Type B	Type A	Type B
R. McK.	4 mos.	< 8	8	128	256	>16	32
J. J.	4 mos.	64	32	128	128	2	4
M. D.	5 mos.	32	32	512	512	16	16
R. M.	5 mos.	32	16	128	64	4	4
J. T.	6 mos.	8	32	64	128	8	4
V. M.	8 mos.	< 8	< 8	8	16	> 0	> 2
B. W.	9 mos.	< 8	<16	32	64	> 4	> 4
E. T.	10 mos.	8	8	32	32	4	4
M. P.	10 mos.	16	8	64	64	4	8
M. O'B.	10 mos.	8	16	32	64	4	4
R. F.	1 yr.	32	32	64	128	2	4
H. O.	1 yr.	8	< 8	128	256	16	>32
S. B.	1 yr.	< 8	< 8	64	64	> 8	> 8
H. T.	1½ yrs.	8	8	<128	< 64	> 8	> 4
S. R.	1½ yrs.	64	8	128	32	2	4
H. R.	1½ yrs.	< 8	8	16	16	> 2	2
B. S.	2 yrs.	8	8	128	128	16	16
C. C.	2 yrs	8	8	64	16	8	2
P. B.	2½ yrs.	8	8	<256	< 64	>16	> 4
J. B.	3 yrs.	8	8	<256	32	>16	4
M. G.	3½ yrs.	< 8	< 8	32	128	> 4	>16
P. P.	3½ yrs.	< 8	< 8	<128	256	16	>32
M. Z.	3½ yrs.	< 8	< 8	32	128	> 4	>16
R. O.	4 yrs.	< 8	8	128	32	>16	4
D. F.	4 yrs.	< 8	8	128	< 64	>16	> 4
J. A.	4 yrs.	16	32	256	256	16	8
A. M.	4½ yrs.	< 8	< 8	32	32	> 4	> 4
J. F.	4½ yrs.	16	32	128	64	8	2
A. G.	4½ yrs.	16	< 8	128	< 32	8	4
G. S.	5 yrs.	32	< 8	<1024	32	>16	> 4
J. R.	5 yrs.	32	16	64	32	2	2
S. K.	5 yrs.	16	8	1024	<128	64	> 8
E. L.	5 yrs.	32	16	128	16	4	0
R. T.	5 yrs.	16	<16	64	< 64	4	4
D. I.	5½ yrs.	8	8	32	16	4	2
J. Mc.	5½ yrs.	< 8	8	16	32	> 2	4
C. S.	5½ yrs.	32	16	256	512	8	32
K. G.	6 yrs.	32	32	128	64	4	2
R. L.	6 yrs.	16	8	32	32	2	4
L. O.	6 yrs.	<16	< 8	128	16	> 8	> 2
F. R.	6 yrs.	16	16	64	256	4	16
K. R.	10 yrs.	16	32	<1024	256	32	8
J. A.	10 yrs.	16	8	256	256	> 8	32
J. B.	10 yrs.	64	128	128	256	2	2
E. J.	10½ yrs.	64	32	256	64	4	2
G. D.	11 yrs.	128	32	256	128	2	4
K. K.	11 yrs.	64	32	256	128	4	4
M. W.	11 yrs.	128	32	512	64	4	2
H. B.	13 yrs.	128	64	<512	256	> 2	4

various subjects cannot be compared. The fold increase in titer is a stable figure and may be used to compare the response produced in all subjects.

Table II presents a summary of the mean fold increase in titer for the various age groups. Considering a 2-fold increase in titer of doubtful significance and a 4-fold or more increase as an indication of adequate immunity to influenza, it is seen that 68% of the children in the 4 mos. to 2 yr. old group produced a good response to type A and 81% to type B. In the 2 to 5 yr. old group, 100% developed a 4-fold or more increase in titer to type A and 61% to type B. Thus, of the children under 5 yrs. of age, 82% developed adequate immunity to type A and 72% to type B. In the 5 to 13 yr. old group, 70% developed adequate immunity to type A and 65% to type B.

TABLE II

MEAN FOLD INCREASE IN SERUM ANTIBODY TITERS AFTER INTRACUTANEOUS INJECTION OF INFLUENZAL VACCINE

Age Group	Number	Mean Fold Increase
Type A Vaccine		
Under 2 yrs.	16	4.55
2 yrs. to 5 yrs.	13	9.90
5 yrs. and over	20	5.10
Type B Vaccine		
Under 2 yrs.	16	5.66
2 yrs. to 5 yrs.	13	6.13
5 yrs. and over	20	4.14

One child of 8 mos. failed to produce any response to type A and another child of 5 yrs. did not produce a response to type B.

REACTIONS

The incidence of reactions was low as would be expected with intracutaneous injections. A few of the older children complained of some burning when the vaccine was injected, but on the whole it was no worse than the discomfort produced by a Schick test. Most of the children developed some erythema about the site of injection, but it disappeared within the first 24 hrs. About half of the children under 5 yrs. of age had a fever of 37.8° to 38.1° C. at some time during the first 24 hrs. One child of 4 yrs. had a temperature of 40° for about 4 hrs. and 8 had temperatures up to 38.8° C. One child's temperature went up to 38.8° to 39.4° and remained there for 2 days, but the pharynx was red and the child appeared to have an upper respiratory infection.

DISCUSSION

While the results obtained in children do not compare with those obtained by Van Gelder[20] and his coworkers in adults, they are significant in that they demonstrate that the majority of children will respond to the intracutaneous injection of influenzal vaccine by increasing the amount of serum antibodies at least four times over the prevaccination level. Because of the low incidence of reactions to the intracutaneous injections and the slight chance of producing allergic reactions, it would be a more suitable method for immunizing large groups of children. The subcutaneous injection of influenzal vaccine produces severe reactions in some children. In a series of 309 patients from 2 months to 15 years who were immunized by the subcutaneous injection of influenzal vaccine, 36% had mild reactions and 5.5% severe reactions (fever of 38.8° or more).[23] One child of 11 months developed convulsions and a temperature of 40° C.

Further work must be done to substantiate the results obtained in this report and to

determine if multiple injections are more satisfactory in children than in adults. It has been suggested that the intracutaneous injection acts only as a booster to stimulate immunity which the individual developed previously through exposure to influenza, and that therefore the basic immunization must be produced by means of subcutaneous injections. If this were true, the subcutaneous injection of the vaccine should have produced much higher antibody titers than were obtained using the intracutaneous route.

Cohen and Schneck[12] obtained no response in children under 2 years of age and the mean fold increase in type A titer for the 2 to 7 year group was 8.5 times and for type B, 23.3 times. In the 7 to 10 year old group they produced a mean fold increase in type A titer of 7 times and type B, 10.5 times.

Larger groups of children must be studied to determine the merits of the intracutaneous and subcutaneous injections. No definite conclusions can be drawn from this study except that it has shown that infants will develop an immune response to the intracutaneous immunization.

Summary

Forty-nine children from 4 months to 13 years of age were immunized by a single intracutaneous injection of influenzal vaccine. An immune response, as indicated by the increase in serum antibody titer, was produced in 99% of the children. The response in the group below 2 years of age was greater than previously reported responses to the subcutaneous injection of influenzal vaccine.

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SPANISH ABSTRACT

Vacuna de Influenza: Efecto de la Inmunización Intracutanea en Infantes y Niños

Se les puso la vacuna de influenza de 0.1 mg. tipos A y B. intracutaneamente a cuarenta y nueve niños de 4 meses a 13 años de edad. Los títulos de anticuerpo de suero fueron determinados antes de la inmunización y de nuevo cuatro semanas después de la inmunización. Considerando un aumento cuatro veces mayor en el título de anticuerpo de suero una indicación del desarrollo de una inmunidad adecuada, se encontró que en los grupos de cuatro meses y dos años de edad el 68% dieron una buena respuesta al tipo A y 81% al tipo B. En el grupo de 2 a 5 años 100% dió una respuesta adecuada al tipo A y 61% al tipo B. En el grupo de 5 a 13 años de edad 70% produjo una buena respuesta al tipo A y 65% al tipo B. Las reacciones a la inyección intracutanea de la vacuna fueron suaves y de poca consecuencia.

Milwaukee County Hospital

MANAGEMENT OF INTRATHORACIC NERVE TUMORS IN YOUNG CHILDREN

Report of Four Cases

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PRIMARY nerve tumors are one of the commonest neoplasms of the posterior mediastinum in all age groups. These neurogenic tumors arise principally from the expected nerve elements present in this location, usually following the sympathetic chain or the intercostal nerves. Since it has been reported[1,2] that approximately 40% of neurogenic tumors are malignant, early excisional surgery is indicated even though the patient is without symptoms.

Kent[1] published an exhaustive review of the world literature up to 1944 on the surgical management of intrathoracic neurogenic tumors. He collected 105 cases from the literature and added 18 cases that had been operated upon at Barnes Hospital. Three of these 18 patients were children younger than 10 years; all three were operated upon but in only one was the tumor completely excised to cure the patient. Tissue studies in the two inoperable cases revealed malignant neurogenic neoplasms. In the 105 collected cases, Kent reports the incidence of malignancy to be 37%. Twenty-five patients of this group were 10 years of age or younger. Only 9 of the 25 (36%) were benefited by surgery; 16 (64%) died after operation because of an inoperable tumor.

Blades' report[3] (1946) of 109 mediastinal tumors that were surgically removed in Army Thoracic Surgery Centers included 29 cases of benign nerve tumors. Geschickter's[2] report of the 850 nerve tumors studied at the Johns Hopkins Hospital indicates that 41% were malignant. The number of mediastinal nerve tumors included in this series is not stated but it is reasonable to assume that it would be small. Nevertheless, the findings of 41% incidence of malignancy compares with the figures of Kent, 37% of the collected cases being considered malignant as were 41% of the Barnes Hospital series. These figures are considered for all age groups, there being no apparent variation in children.

There is a paucity of literature pertaining to neurogenic intrathoracic neoplasms in children, most of which consists of individual case reports and too few reported series of significant number to establish conclusions. However, it is apparent that neurogenic intrathoracic tumors are not infrequent in children and have been found at birth. Higgins[4] reports one case of an infant who died at the age of one month due to a neurogenic tumor in the right posterior mediastinum.

It is of particular significance that Blades,[3] Kent[1] and Adams[5] and other writers have repeatedly emphasized that the treatment of intrathoracic nerve tumors is surgical. It has been demonstrated repeatedly that roentgen therapy has little place in the treatment of a primary nerve tumor. Since these neoplasms are associated with an over-all 40% incidence of malignancy, there would seem to be little justification in prolonged observation or

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procrastination. As yet there is no reason to assume that the management of an intrathoracic neoplasm in the child should differ from that in the adult. Kent advises that the roentgenologic evidence of a shadow in the posterior mediastinum in any age group, regardless of absence of clinical symptoms, should be considered as most likely due to a neurogenic tumor. It follows that this presumption alone is an indication for an exploratory thoracotomy.

Case Reports

Four case histories are reported at this time. All the patients were children under six years of age. In each case, the child was subjected to roentgenologic study of the thorax after a physical examination and a roentgen shadow in the posterior mediastinum was detected. The clinical diagnosis of a neurogenic tumor was made and later confirmed by tissue study of the surgical specimen. All four children are enjoying excellent health and are apparently cured.

Case 1. L.T. Aged 5½ yrs., white female. On admission to the hospital, patient had a functional heart murmur that was 1st discovered at the age of 2 yrs. Three mos. previously, a cardiologist

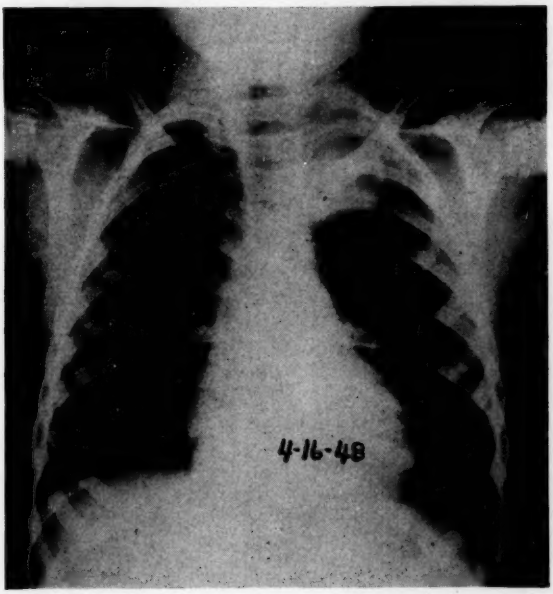

Fig. 1. Case 1. Chest roentgenogram demonstrates sharply circumscribed apical tumor which fluoroscopically was located in posterior mediastinum.

detected a mass in the left posterior mediastinum during fluoroscopic and roentgen examination (Fig. 1). There were no objective or subjective symptoms related to the tumor except the finding of cafe-au-lait spots over the body, the significant stigmata of neurofibromatosis. Her father has similar spots and a small lump in the neck. The day after admission, an exploratory thoracotomy was performed and a retropleural mass found in the left apical region. The inferior border of the tumor was at the level of the 3rd rib posteriorly and the mass extended up into the 1st rib circle. The neoplasm was soft, encapsulated and apparently intimate with the sympathetic chain. However,

the tumor extended by finger-like projections beyond the 1st rib into the neck. The blood supply appeared to arise from 2 branches of the subclavian artery and a 3rd vessel that descended from the neck. The entire mass was dissected out within its capsule. Patient had an uneventful postoperative period except for a left Horner's syndrome which improved considerably within 3 mos. The pathologist reported the tumor to be a neurofibroma. Patient is well and the chest is clear several mos. after operation (Fig. 2).

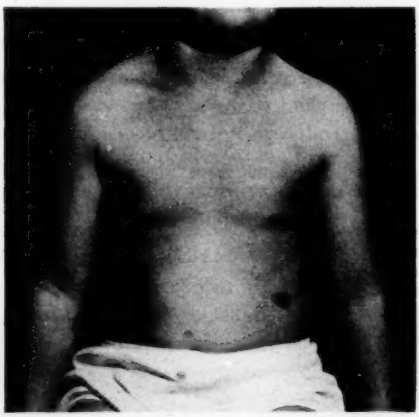

FIG. 2. Case 1. Photograph of patient 3 mos. postoperatively shows persistent cafe-au-lait spots and absence of thoracic deformity.

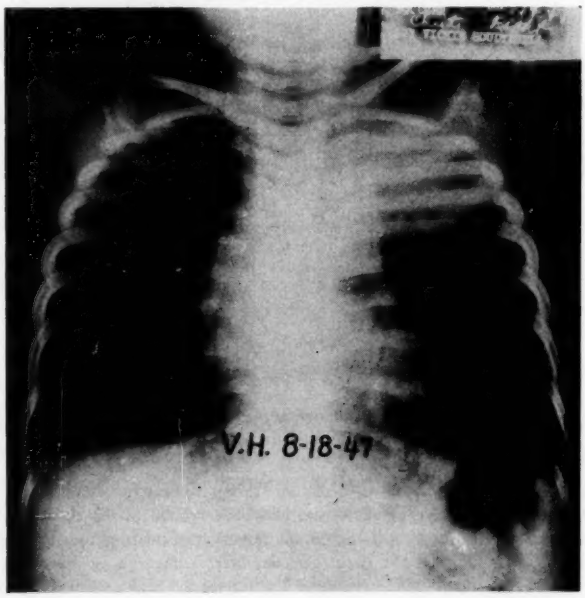

FIG. 3. Case 2. Preoperative roentgenogram reveals tumor in left upper thorax containing small flecks of increased densities simulating particles of calcium. Findings were confirmed at operation.

Case 2. V.H. Aged 2½ yrs., white female. Patient was 1st admitted to the hospital in Sept. 1947 for study. She had recovered from pertussis but the cough had persisted. A roentgenogram of the chest (Fig. 3) revealed an apical tumor which was located in the left posterior mediastinum by lateral roentgenogram. Biopsy of a cervical node revealed lymphoid hyperplasia. She was discharged because of skin rash and advised to return. The child was apparently in good health after the discharge and the cough disappeared. On Jan. 13, 1948, she was readmitted for surgery. Examination revealed a normal child of 2½ yrs. The following day an exploratory thoracotomy was performed and a long segment of the 4th rib resected. A smooth mass was firmly attached to the posterior chest

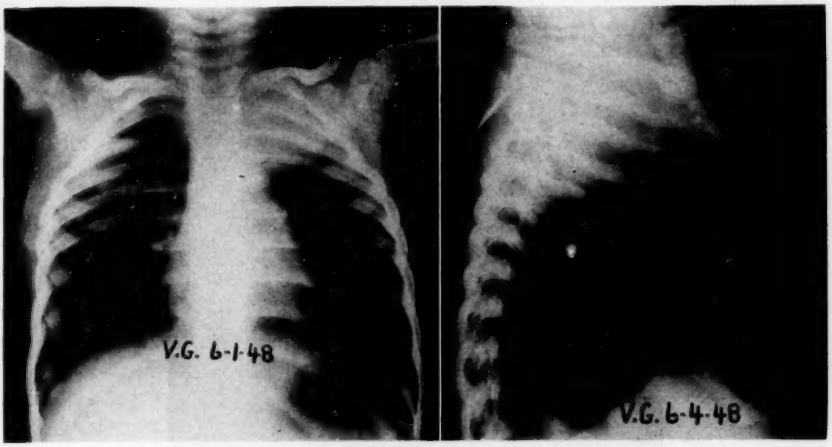

FIG. 4 FIG. 5

FIGS. 4 and 5. Case 3. Anteroposterior and lateral roentgenograms disclose tumor in left apical posterior mediastinum.

wall. It was dissected out after the ligation of several branches of intercostal arteries. The tumor had eroded the 2nd and 3rd ribs in the costovertebral gutter and seemed to follow the nerves into the intervertebral foramina. The entire tumor was grossly removed. The child made an excellent recovery except for a left Horner's syndrome which subsequently cleared. The Dept. of Pathology reports identified the tumor as ganglioneuroma; no evidence of malignancy was noted.

Case 3. V.G. Aged 2½ yrs., white male. The child's mother stated that he would "gag" whenever clothing or other objects touched his throat. This symptom persisted for about 1 mo. and no other complaints were recorded. At the mother's insistence, roentgenograms of the chest and neck were made (Figs. 4 and 5). An apical posterior mediastinal tumor was discovered in the left hemithorax. Physical examination was normal in all respects and additional laboratory studies revealed no evidence of abnormality. Left thoracotomy was performed and a large mass observed in the upper posterior mediastinum. The tumor was retropleural, extending from the level of the 4th rib into the 1st rib circle. Three branches of the subclavian artery entered the mass and a branch of the highest intercostal vein could be identified as leaving the capsule. The tumor was dissected out of the mediastinum. Recovery was uneventful except for a left Horner's syndrome. This complication showed complete resolution in 3 mos. except for the miosis. The Dept. of Pathology report identified the tumor as ganglioneuroma; no evidence of malignancy was noted.

Case 4. E.D.C. Aged 4 yrs., white female. The child was admitted to the hospital for treatment of a probable neurogenic tumor. The neoplasm was suspected after a roentgenogram of the thorax (Fig. 6) during clinical studies for an unrelated condition. There were no objective or subjective clinical findings relative to the tumor. Patient appeared to be perfectly normal in all respects. Exploratory thoracotomy was performed by Dr. Brian B. Blades (assisted by D.B.E.) and the tumor removed. The neoplasm was found to be retropleural in the posterior mediastinum between the 3rd

rib and the 8th rib posteriorly and apparently arising from the sympathetic chain. The postoperative period was uneventful and the patient is well. The Dept. of Pathology report was ganglioneuroma, benign.

Discussion

Primary nerve tumors of the posterior mediastinum occur in all age groups. The incidence of occurrence and the degree of malignancy are essentially the same in children as in adults. For this reason, the roentgen finding of a posterior mediastinal tumor in a child must be viewed with some degree of apprehension. There seems to be no question that

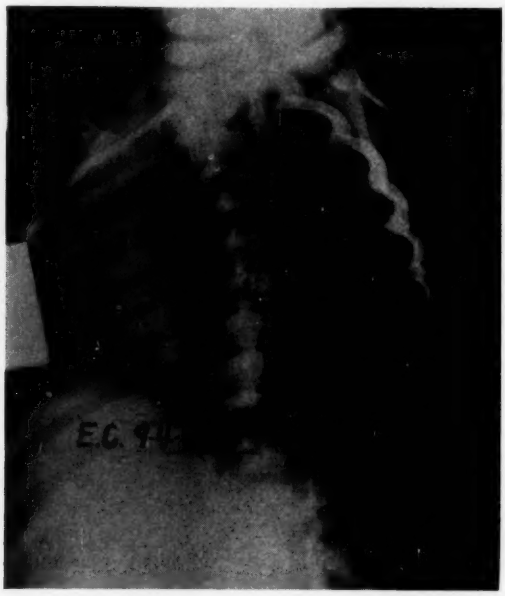

Fig. 6. Case 4. Oblique roentgenogram outlines tumor mass in left posterior mediastinum.

exploratory thoracotomy is the most important procedure in the diagnosis and the management of a suspected intrathoracic nerve tumor.

Treatment

Exploratory thoracotomy in the apparently healthy child is a relatively innocuous procedure and the over-all mortality rate should not be higher than for laparotomy. The operative procedure was essentially the same in the four cases presented. Anesthesia was administered by a closed endotracheal system, employing nitrous oxide, oxygen and ether. In each case a posterolateral incision was made and the fourth, fifth or the sixth rib resected subperiosteally. It is rarely necessary to resect more than one rib or to cut adjacent ribs. Excellent exposure was obtained with a Tuffier or Rienhoff rib spreader. As these tumors are usually retropleural, it is necessary to incise the overlying parietal pleura; in the superior mediastinum, it may be necessary to ligate and divide the highest intercostal vein. In most cases the tumor is intimate with the sympathetic chain or intercostal nerves; rarely does a primary nerve tumor arise from the vagus nerve. The benign neoplasm is

usually dissected out with little difficulty unless it extends beyond the first rib circle into the neck, as occurred in three of the cases presented here. Usually the blood supply to the tumor is obvious and bleeding can be safely controlled. The malignant neurogenic tumor presents a formidable problem and is noted for its associated high incidence of inoperability. Usually the closure is simple and is accomplished without drainage after re-expansion of the lung. Intercostal drainage may be employed when the surgeon anticipates bleeding or effusion from an extensively denuded area.

Complications

The complications of thoracotomy in the child include hydropneumothorax, atelectasis and hemothorax; these should be recognized promptly by the physical and roentgen findings. Early thoracentesis or tracheal aspiration will give prompt relief. Empyema is now a rare complication due to the refinement of surgical technic and the routine use of chemotherapy and antibiotics in the postoperative management.

An expected postoperative complication in the patient who has a high posterior mediastinal tumor is a residual Horner's syndrome on the ipsolateral side. Since these tumors arise from, or usually involve, the superior thoracic sympathetic ganglia, it is usually necessary to sacrifice this tissue to insure complete excision of the tumor. Although a true Horner's syndrome results, there is eventual improvement in the function of the palpebral muscles; only the pupil inequality need be permanent. This expected complication in the child with a neurogenic tumor in the superior posterior mediastinum is scarcely of enough significance to influence the management of the problem. Nevertheless, it is well to inform the parents of this expected complication prior to the surgery.

The most serious long range complication is recurrence of the tumor. Blades expresses the opinion held by many surgeons and pathologists who believe that recurrence of an inadequately excised neurogenic tumor is accompanied by a higher incidence of malignant degeneration. It is of greatest importance therefore that a thorough, painstaking effort be made to remove every vestige of the gross tumor mass. Early excisional surgery is therefore advocated regardless of the age of the infant or child.

Summary

A brief review of the literature referring to intrathoracic nerve tumors in children is presented. The neurogenic tumors have an expected incidence of malignancy of about 40%.

Four case histories are reported in which neurogenic tumors of the posterior mediastinum were removed with apparent cure. Only one of these children had objective or subjective signs which could be attributed to their neoplasms. All of the neoplasms were benign.

Prompt thoracotomy is advocated in the child with a suspected neurogenic tumor of the mediastinum. Periods of observation, procrastination and roentgen therapy are to be condemned for it is impossible to predict with any degree of certainty which tumor will or already has undergone malignant changes. A brief discussion of the operative management and complications is presented.

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SPANISH ABSTRACT

Manejo de Tumores del Nervio Intratoracico en Niños Pequeños

Se presenta una breve revista de la literatura referente a tumores del nervio intratorácico en los niños. Los tumores neurogénicos tienen una incidencia supuesta de malignidad de aproximadamente el 40%.

Se han reportado cuatro casos en los cuales se removieron tumores neurogénicos del mediastino posterior con aparente cura. Solamente uno de estos niños tenía signos objetivos o subjetivos que podían ser atribuídos a sus neoplasmas. Todos los neoplasmas fueron benignos.

Se recomienda una pronta toracotomía en el niño que se crea tenga un tumor neurogénico del mediastino. Hay que condenar los períodos de observación, demora y terapia roentgen, pues es imposible pronosticar con certeza cual es el tumor que sufrirá o ha sufrido ya cambios malignos. Se presenta una breve discusión sobre el manejo operativo y las complicaciones.

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NEVOXANTHO-ENDOTHELIOMA WITH OCULAR INVOLVEMENT

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NEVOXANTHO-ENDOTHELIOMA, an unusual type of cutaneous tumor, was first described by Adamson[1] in 1905 and publicized by McDonaugh[2] under its present name. Although rare, the disorder has been receiving considerable attention in recent years.[3, 4]

Nevoxantho-endothelioma consists of multiple growths in the skin, which have a reddish to yellow color. The tumors may be present at birth or may not appear until later. There may be a history of other cases in the family. The lesions have a predilection for the face and scalp, and usually tend toward spontaneous cure, although they may persist for years. Occasionally they begin as red tumors, like angiomas, and become yellow later. No significant changes have been found in constitutional studies of carbohydrate and fat metabolism. The histologic picture of the cutaneous lesions is characteristic and distinctive, yet is often mistaken for sarcoma, degenerative neurofibroma, or one of the histiocytic infiltrations such as generalized xanthomatosis (Hand-Schüller-Christian disease). As summarized by McDonaugh, the lesions are dense cellular growths, possibly originating from the capillary endothelium. The endothelial-like cells disappear as newly-formed connective tissue takes their place. Also present are giant cells which do not always resemble ordinary Touton giant cells, but in fresh preparations can be demonstrated to be made up of syncytial aggregates of endothelial cells. McDonaugh felt that these tumors represented a nevus formed by an overgrowth of embryonic mesenchymal cells or endothelial cells, and that the xanthoma-like condition results from fatty changes in the cells during their dissolution. Senear and Caro[4] lean to the view that the lesions are actually those of the juvenile xanthoma group. The lesion is evidently a nevus (in the sense that it is a "circumscribed new growth of the skin of congenital origin"[5]) with added xanthomatous changes, but many workers have felt that it is neither juvenile xanthoma nor endothelioma. Present understanding of the pathogenesis of the disease does not go much further than this.

The published reports rarely describe associated visceral changes. Lamb and Lain[3] noted apparent systemic involvement in their case, and Ellis, in discussion of this case, cited ocular involvement in a patient of Simpson and Anderson, but he presented no histologic evidence to indicate the nature of the eye disease. In view of the apparent rarity of nevoxantho-endothelioma, this paper reports a unique example in which an associated ocular lesion was pathologically similar to the associated cutaneous changes.

CASE REPORT

A Negro boy aged 4 mos. was admitted to The Children's Hospital of Philadelphia. Five days earlier it had been noted that he seemed to be keeping his left eye closed and had mild photophobia. No changes had been noted in the eye nor did he attempt to rub it.

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Past medical history revealed that the infant had a normal spontaneous delivery at term. The mother had had no diseases during pregnancy. No asphyxia or birth injury had occurred. Development and nutritional history were not remarkable.

The child was healthy, without any apparent disease of the skin, head, lymph nodes, trunk, extremities or internal organs, apart from the left eye. Examination of the left eye (confirmed under general anesthesia) revealed slight edema of the lids, narrowing of the palpebral fissure, moderate epiphora and injected conjunctiva. The continuity of the iris was interrupted in the lower quadrant by an easily visualized pigmented mass. Because light was not transmitted through the orbit, the fundus could not be visualized. This was thought to result from increased ocular tension. The right eye was normal. It was felt that the patient had a primary sarcoma of the left eye, with secondary glaucoma. The eye was enucleated 1 wk. after admission. No other lesions were found at operation,

FIG. 1. Isolated firm papule in skin of abdomen at time of 2nd hospital admission.

and the eye was prepared for microscopic examination. Patient was discharged 1 wk. later, after an uneventful postoperative course.

Laboratory studies during this admission included a negative serologic reaction for syphilis, a negative tuberculin skin test and normal roentgenogram of the chest. Blood count showed 12 thousand leukocytes, with 34% neutrophiles, 60% lymphocytes, 14% monocytes, 2% eosinophils and Hgb. 12.0 gm. Urine showed no microscopic or chemical abnormalities.

Although he seemed in good health and had gained weight, the patient was rehospitalized about 4 mos. later because of numerous skin lesions over his head and trunk. These began to appear about 3 wks. before admission. They were asymptomatic and came out singly and in crops and at first were thought to be metastases from the eye lesion. Physical examination was completely normal, except for a prosthesis in the left orbit and the skin findings. Several widely separated lesions approximately 1.5 cm. in diameter were noted on the skin of the abdomen (Fig. 1) and left thigh, and similar lesions from 0.5 to 1.5 cm. in diameter were studded over the left frontal and parietal areas. The nodules were discrete, round, firm and reddish-tan in color, and were covered by smooth epidermis suggestive of a noninflammatory neoplastic process. They had a broad base and were elevated to 2 to 10 mm. above the surrounding skin. One of the lesions of the scalp was removed for microscopic study.

Studies of the blood cells, blood chemistry (sugar and cholesterol), bone marrow and urine yielded normal findings. Roentgenograms of the chest, skull and long bones showed no abnormalities. The biopsy site healed uneventfully and the patient was discharged in apparent good general health. No specific therapy was given. At the time of a follow-up examination 6 mos. after discharge, the boy was found to be growing normally. Some of the cutaneous lesions had disappeared and a few additional ones had appeared. Eleven mos. after discharge, the patient's new guardian reported by telephone that he was in apparent good health. Although a number of cutaneous lesions were present, they seemed to be flattening out.

Skin.—The specimens consisted of 2 small elliptic areas of scalp, each containing a yellow raised area respectively 0.5 and 0.25 cm. in diameter. The tissues cut easily, and the cut surface of

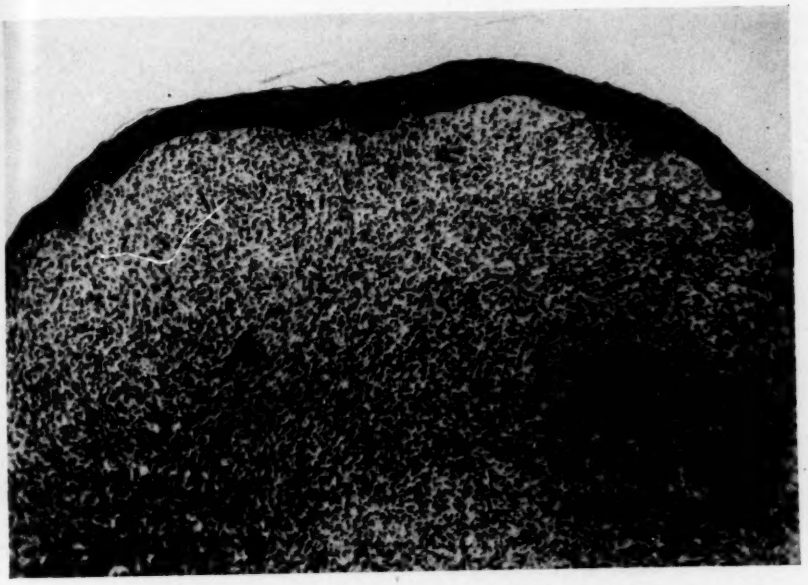

FIG. 2. Biopsy of skin lesion showing atrophy of epidermis and massive cellular infiltrate in corium. (H & E × 80)

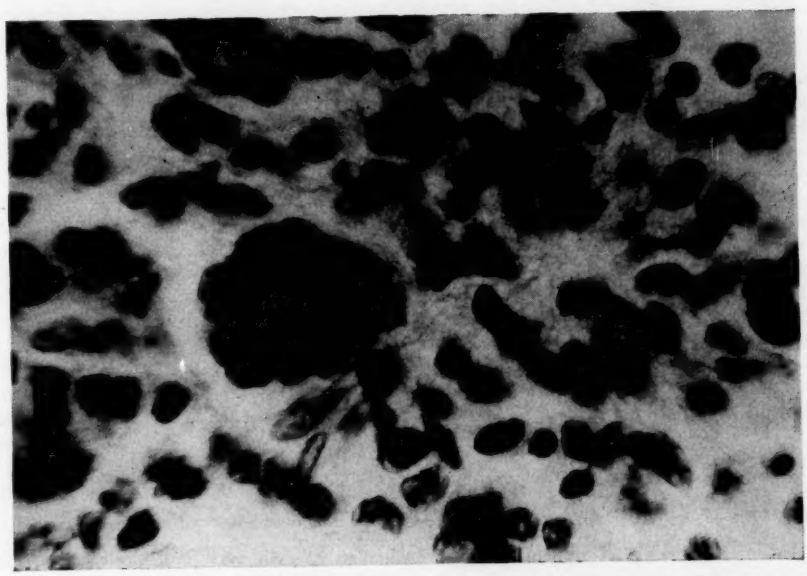

FIG. 3. High power of section in Fig. 2. Touton giant cell seems to consist of nuclei arranged in ring. (H & E × 900)

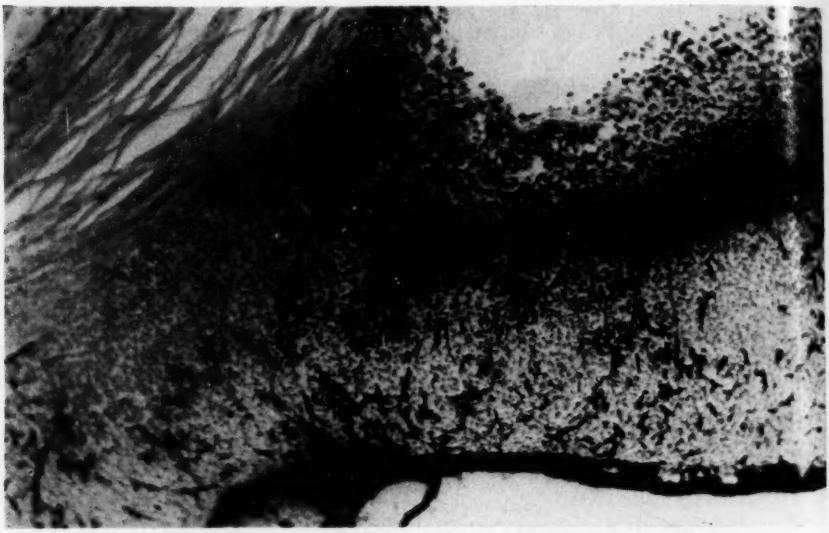

FIG. 4. Section of eye including iris and cornea. Infiltrating cells fill iris but are sharply limited at cornea. (H & E × 80)

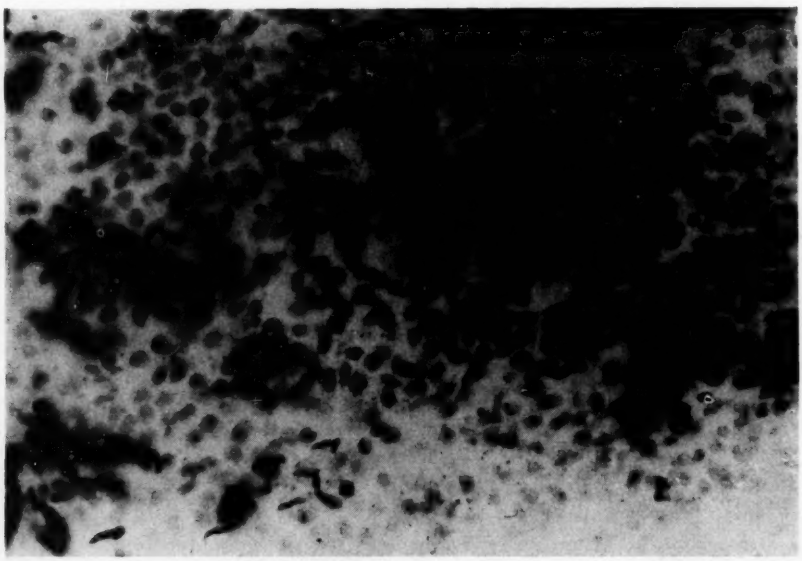

FIG. 5. High power of section in Fig. 4. Infiltrating cells fill most of iris between melanin granules. There are several distinct Touton giant cells comparable to those in skin sections. (H & E × 600)

the lesions was yellowish white. Grossly, the yellow tissue appeared to be well demarkated from the scalp structures.

Both pieces of skin were identical on microscopic examination (Figs. 2 and 3). The epidermis overlying the lesion was thinned, and the rete pegs were blunted, shorter and fewer in number than in the adjoining area. The stratum germinativum was sharply defined and nowhere was encroached upon by the underlying cells. All recognizable structures of the corium had been replaced by the invading cells, except for a few small blood vessels of capillary size and scanty strands of collagenous tissue.

The cells which made up the mass of the lesion were arranged in short strands and whorls, with no apparent regular or consistent pattern. The nuclei stained well along their periphery with hematoxylin, but appeared generally vesicular. The chromatin was condensed into one or more small dark granules. There was considerable variation in nuclear size and shape, but the majority of nuclei were oval and approximately 10 to 12 μ in length. Their long axis was parallel to that of the neighboring nuclei. The cytoplasm stained lightly with eosin and had a granular or globular pattern, but no cytoplasmic or cell boundaries could be determined.

Scattered throughout the mass were some Touton giant cells. These had approximately 10 to 16 nuclei, arranged closely in a ring or rosette-like group around the periphery of an area of eosinophilic cytoplasm. A few eosinophilic granulocytes were seen but no other inflammatory cells or reactions were recognized in or surrounding the nodule.

The lower boundaries of the lesion were not distinct; small nests and strands of cells were seen infiltrating the marginal corium and the underlying adipose tissue. A rare mitotic figure was recognized. Sections stained by the Kolmer-Boerner reticulum stain showed a loss of normal reticular structure of the corium in the involved area.

Eye.—The enucleated eye was fixed in formalin and sectioned, after preparation by the celloidin technic. The sections included the entire bulb, and transsected the center of the bulb in the horizontal plane. Hematoxylin and eosin were used to stain the tissues.

Histologically, all structures appeared normal except those of the ciliary bodies and the irides (Fig. 4 and 5). The ciliary bodies and their processes and the irides anterior to the posterior facies were infiltrated and partially replaced by large numbers of invading cells. The stratum pigmentosa of the ciliary body and the pigmented posterior epithelial linings of the iris were intact. The canal of Schlemm was not identifiable on either side of the eye. The sphincter muscle fibers were not discernible. All of the iris anterior to the pigmented layer was composed of invading nevus-like cellular proliferation, except for a line of pigment which extended the length of the iris, and scattered pigment granules on either side of this. The iris was thickest distal to its attachment to the bulb. The anterior surface of 1 portion showed a small extravasation of erythrocytes of recent origin. Evidence of older hemorrhages was seen in the many macrophages in this area, which contained golden yellow pigment. Inflammatory cells of other types, including polymorphonuclear neutrophils, eosinophils and small round cells, were present. Many unrecognizable degenerated forms were seen in this portion of the iris contiguous to the anterior chamber.

The nevus cells showed no visibly stained cytoplasm. In arrangement and morphology, their nuclei were identical with those in the skin lesions. The nuclei were vesicular, faintly basophilic and contained one or more areas of condensed chromatin. They were mostly oval in shape and arranged parallel to one another. The multinucleated or Touton forms were also present within the body of the infiltrate in the iris. Few mitotic figures were seen. The lesion did not display malignant characteristics: growth was relatively orderly and the neighboring structures were not invaded to any significant degree. Comparison of the sections of the cutaneous lesion and of the eye lesion demonstrated their identity under the microscope.

Conclusions

Nevoxantho-endothelioma is a benign nevus with xanthomatous changes. It appears at birth or shortly thereafter. The process may occasionally be mistaken for sarcoma, but usually follows a benign course with crops of new lesions which eventually tend toward spontaneous involution. This case demonstrates that the eye can be involved by lesions having the same histologic structure as those of the skin. Because of the favorable course

of patients suffering from this disease and the realization that visceral lesions may occur in nevoxantho-endothelioma, early diagnosis insures an accurate favorable prognosis.

ACKNOWLEDGMENT

Acknowledgment is made to Dr. Wilfred E. Fry, Wills Hospital, Philadelphia, Pa., for the preparation of the sections of the eye.

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SPANISH ABSTRACT

Endotelioma-Nevoxanto con Complicación Ocular

El endotelioma-nevoxanto es un nevo benigno con cambios xantomatosos. Aparece al nacer o poco después. El proceso puede algunas veces confundirse con sarcoma; pero generalmente sigue un curso benigno con producción de nuevas lesiones, las cuales con el tiempo tienden a involución espontanea. Este caso demuestra que el ojo puede ser afectado por lesiones que tienen la misma estructura histológica que las de la piel. A causa del curso favorable de pacientes que padecen de esta enfermedad y la realización de que las lesiones viscerales pueden ocurrir en el endotelioma-nevoxanto, una diagnosis temprana asegura un pronóstico favorable correcto.

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BRONCHIECTASIS IN CHILDHOOD

III. Prophylaxis, Treatment and Progress with a Follow-up Study of 202 Cases of Established Bronchiectasis

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THE clinical and aetiologic aspects of bronchiectasis in children have already been discussed in Parts I and II (Field[1,2]). The purpose of this paper (Part III) is to record the experiences resulting from a careful follow-up of 202 children with proved bronchiectasis over a period of 10 years and to discuss the treatment recommended. Undoubtedly, as the period of observation increases further knowledge will be gained, and many conclusions arrived at from present facts may have to be adjusted. Nevertheless, from present knowledge, it seems justifiable to state that with better social conditions and prophylactic care much irreversible bronchiectasis can be prevented while with judicious treatment and skilled surgery many children can be cured. Even with simple medical treatment the progress of most cases can be arrested, some showing considerable improvement and a few being clinically cured although the bronchograms show persistent bronchiectasis. More rarely in mild cases the bronchographic picture over the years may show regression or actual recovery in what appeared to be irreversible bronchiectasis.

PROPHYLAXIS

Irreversible bronchiectasis is not commonly seen in the better social and economic classes. Good nutrition and home conditions probably give the child a better chance of more complete recovery from the lung damaging diseases, and many children in the upper social classes may be sent away for a holiday to recover from a severe attack of pneumonia, pertussis or rubeola, whereas a child in the lower social classes may have to convalesce in a small, badly ventilated room or on the streets. Therefore, better home conditions and more facilities for convalescence following acute respiratory diseases is a first consideration in the prevention of bronchiectasis.

As pneumonia and pertussis are the chief predisposing diseases to bronchiectasis (Field[1,2]), prevention of these diseases or better treatment ought to reduce the incidence of bronchiectasis. Improved treatment is at present our only weapon in pneumonia. Adequate chemotherapy followed by a good period of convalescence preferably in the country or by the sea is important. Where pulmonary secretions are tenacious and difficult to cough up, steam inhalations or a period in a steam tent may help drainage. The success of prophylactic pertussis vaccines has been reported by Sauer[3] in America and others; the same success has not been achieved so far in England (McFarlan, Topley and Fisher[4]), but a wide scale investigation by the Medical Research Council is in progress. Nevertheless, it seems justifiable in view of the serious sequelae of pertussis to give the vaccine probably combined with diphtheria inoculation at three to six months of age. If given

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later than this, a number of infants will not be protected at a serious time for permanent lung damage to occur. If given earlier, the development of immunity is poor. Belladonna is contraindicated in the treatment of pertussis, as it dries pulmonary secretions and makes them more sticky and difficult to cough up, thereby predisposing to pulmonary collapse. The treatment of pertussis contacts with hyperimmune human serum has been reviewed by Sauer.[3] It is worthy of trial before the paroxysmal stage has developed. However, it is during recovery that particular care should be taken. Good convalescent care is important in all cases and careful repeated clinical examination of the chest should be made. If

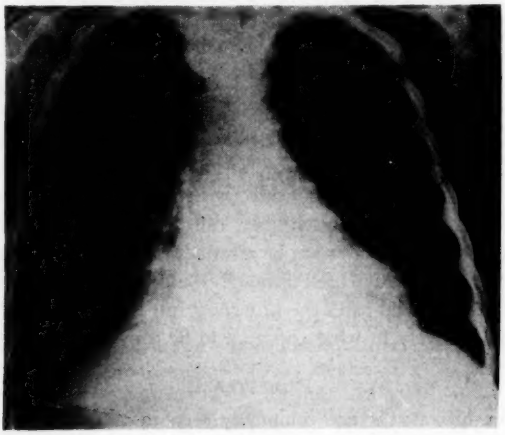


FIG. 1. A-P roentgenogram demonstrating absence of defined margin to basal opacities in lobular collapse of lower lobes.

progress is not satisfactory, roentgenogram should be taken. When pulmonary collapse is present or suspected following pertussis or other diseases, or when pneumonia is slow in resolving, treatment should be instituted without delay, as described in Part II (Field[2]).

The value of bronchoscopic aspiration in prevention of bronchiectasis is difficult to assess. Undoubtedly, it is important where a foreign body is suspected but, as was shown in Part II (Field[2]), its value in pulmonary collapse when compared with good medical treatment and steam inhalations is doubtful. Hart[5] advocates repeated bronchoscopic aspiration for pulmonary collapse. This has been tried on a few of these cases, but the impression gained is that, if the lung fails to expand after the first bronchoscopy, further treatments will be of little avail. For children with a tuberculous hilar gland narrowing or occluding a bronchus, bronchoscopy may be helpful. In some of these cases a little mucus has completed the occlusion and can be sucked out, or granulations may be removed to make an airway to the collapsed lobe beyond. As there is a danger that this latter procedure may later produce stenosis of the bronchus, some surgeons prefer just to pass a catheter through the granulation tissue and suck out any retained secretions beyond. This procedure may require to be repeated as the granulations often grow again.

There remains the indefinite group of cases predisposing to bronchiectasis—asthma with bronchitis and doubtful bronchiectasis so often designated chronic bronchitis. With much retained secretion in the chest there are probably scattered areas of collapse known

as lobular collapse (Fig. 1) so that it is best to institute treatment as for massive collapse for a few weeks. Good convalescent care in a dry climate is frequently helpful.

It has already been shown that nasopharyngeal infection is closely associated with bronchiectasis; the one infection predisposes to the other, yet both can exist separately. In the prevention of bronchiectasis, therefore, it is important to treat infection in the nose and throat at the same time as treating the chest complaint. If the tonsils and adenoids are grossly septic or causing obstructive symptoms, they should be removed, and when mucopus is constantly dripping down the back of the throat it is advisable to treat the antral infection, but it hardly seems justifiable to treat antra that give rise to no symptoms even if they are opaque in the roentgenogram. Extensive surgical procedures on the nose should be deferred, as nasal infection frequently clears when the chest condition improves. To teach the child to blow his nose properly is probably a useful prophylactic measure.

Chemotherapeutic aerosol treatment for the prevention of bronchiectasis requires further investigation before its value can be assessed. Physiotherapy which includes postural drainage, breathing exercises and chest clappings is of considerable help in the prebronchiectatic state.

The importance of convalescent care in the prevention of bronchiectasis cannot be overstressed. Delay in procuring this convalescent care may convert a reversible into an irreversible bronchiectasis and the critical period is in the first six or nine months of the chest trouble. Convalescence should be for at least six months, otherwise there is a real danger of recurrence of symptoms or of pulmonary collapse on returning home.

Treatment

There comes a time in the observation of a case when it is decided that the bronchiectatic condition is irreversible. The deciding factors are the duration of constant cough for a year or more and bronchographic evidence that the dilatations have been present for one or more years. Even then there are certain cases that give rise to doubt, for instance, the case that shows intermittent collapse over the years with varying degrees of bronchial dilatation (Figs. 2-7). In these doubtful cases it is much wiser, before considering operative treatment, to keep the child under close observation and repeat the bronchograms in a year or two when the areas showing irreversible change will be more clearly defined.

When the bronchiectasis is established beyond doubt, a choice must be made of three forms of treatment. 1. A cure may be attempted by radical surgical removal of all diseased parts of the lung. 2. Treatment may be purely medical with the aim of relieving symptoms. 3. If the disease is too extensive for radical surgery, excision of the more grossly diseased parts may be combined with medical treatment for relief of symptoms.

Selection of Cases for Surgery.—In skilled hands, the operative mortality in children is low, and with the introduction of modern anaesthetic methods and chemotherapy complications are considerably reduced so that operative risks can be considered as minimal. The goal to achieve is not necessarily anatomic removal of all diseased parts, but clinical cure of the patient. In some cases it may be possible to remove all the diseased parts but clinically the child is no better, whereas in other cases where no operation has been performed the child—for a time at least—appears to be quite well although the bronchi remain dilated. So far our practice has been to advise operation for all cases with localised bronchiectasis which was not too extensive for complete clinical and anatomic cure. This policy has been adopted for all cases irrespective of the mildness or severity of the symp-

toms, in view of the danger of serious ill health in adult life, but whether such a policy is justifiable when symptoms are controlled or absent requires more prolonged follow-up of cases for proof. Operation may also be advised in cases of diffuse mild bronchiectasis with small segments of advanced dilatation, for removal of the latter may greatly alleviate symptoms. It is contraindicated, however, in cases of uniform generalized bronchiectasis and in those of localized bronchiectasis where not enough healthy segments can be preserved to support active life.

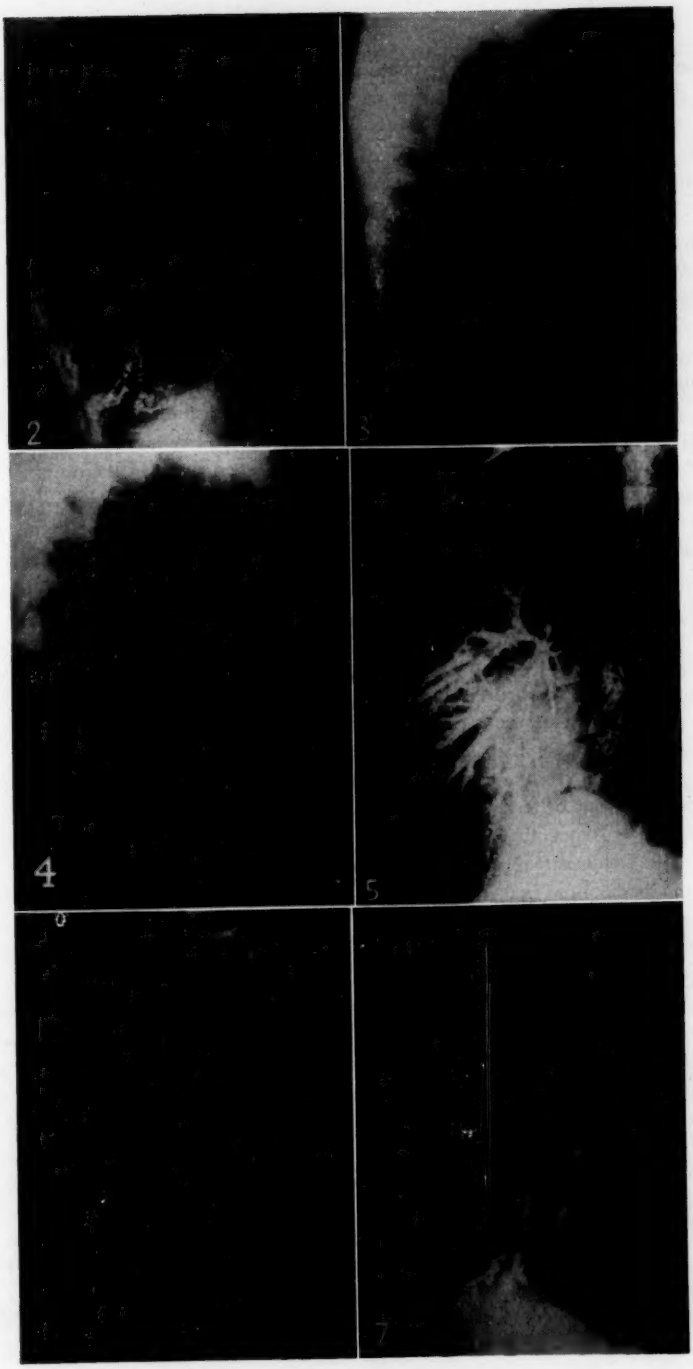
The timing of operation and the planning of multiple operations are matters for individual decision in each case. If the child is not ill there is no urgency. The necessity for precision in diagnosis often requires delay for repeated bronchograms. Sometimes, however, the severity of the symptoms is an indication for urgent operation even when diagnosis by bronchogram is not complete. When symptoms are severe there is usually no doubt about the irreversibility of the bronchiectasis and it is only the extent of the disease that requires definition. Planning the treatment in such a case may be difficult but, if toxaemia is uncontrolled by medical treatment, long delay for the sake of precision in diagnosis may be dangerous.

How Much Lung Can Safely Be Removed.—The preservation of small segments of healthy lung is always worth while in children since growth of the remaining segments undoubtedly takes place. It is recommended, therefore, that where possible segmental resection rather than total lobectomy should be performed (Churchill and Belsey,[6] Pilcher[7]). Children can lead a normal life with two upper lobes only or a right upper and lower lobe or possibly even less than that. However, when such extensive removals are performed it is advisable to leave ample time between operations to enable the remaining lung to enlarge and improve its function. Only in children with gross disease is this extensive removal recommended as some disability and dyspnoea on exertion usually follows and persists—although one child in this series, who was left with a right upper and lower lobe only, is plump and sturdy, has won a scholarship at school and joins in all games; she does, however, get breathless on excessive exertion. It is recommended that if possible half the pulmonary tissue be retained to avoid undue functional disability.

Régime for Medical Treatment.—This can be carried out in the home, at a convalescent home or open air school or even at a boarding school. In early cases where there is a possibility of the condition being reversible or in cases where there may be improvement of general health, an open air school is preferred, but where the condition is chronic it is perhaps best for the child to be treated at home and attend an ordinary school so that minimal adjustments are necessary for an average normal existence. As the child grows older the régime can be relaxed according to progress.

FIGS. 2-7. Bronchograms of girl aged 8 yrs., demonstrating possible reversibility of tubular (cylindric) dilatation and irreversibility of branches showing widened or bulbous periphery as seen in lingula.

Fig. 2. Right lateral bronchogram (1943). Tubular dilatation of RML and possibly of antero-lateral (pectoral) branch of RUL. Fig. 3. Right lateral bronchogram (1945). All branches except lateral branches of RML are now normal. Fig. 4. Right lateral bronchogram (1946). There is now tubular dilatation of right middle, antero-lateral (pectoral) of right upper and possibly of posterior basic branches. Fig. 5. Left oblique bronchogram (1943). There is tubular dilatation of lingula with slightly bulbous periphery. Doubtful dilatation of lower lobe. Fig. 6. Left oblique bronchogram (1945). All visible branches look normal except lingula which shows tubular dilatation with bulbous tip. Fig. 7. Left oblique bronchogram (1948). Lingula is still dilated and has bulbous tip. Lower lobe is now collapsed and shows tubular dilatation not necessarily irreversible.



FIGS. 2-7. See opposite page for description.

Postural drainage over a tipping board in the most advantageous position for drainage of the diseased part is instituted all night (Foster-Carter[8]). Where more than one position is required, the child is turned over during the night. With restless children a restrainer such as the Treloar spinal jacket (Spirella Co.) is worn to maintain the child in position. In the morning chest clappings, particularly over the diseased areas, are given and the child encouraged to cough up the sputum. Chest clappings are repeated in the evening before going to bed after physical exercises. Where conditions permit, a period of rest in the middle of the day with postural drainage followed by chest clappings is an advantage.

Physiotherapy is given as a routine for all. Children living at home are given instruction at hospital in respiratory and postural exercises and the parents then supervise these night and morning in the home. At first it is usually preferable to arrange attendance at a class until the child and parents are familiar with the exercises when a periodic check-up is all that is required. Open air play and sport is encouraged, swimming allowed and the child is encouraged to live as normal a life as possible. In the open air schools, it is an advantage to hold a daily exercise class preferably taken by a resident or a visiting physiotherapist or gymnast. The child's chest is supple so that deformities are more easily corrected and the child taught to take advantage of the good parts of his lung. Success depends on the efficiency and enthusiasm of the physiotherapist and her capacity to impart this enthusiasm to the child.

Fresh air and good food are important factors in most respiratory disorders. Sleeping in the open air is suitable for the majority of cases, but the frequency of upper respiratory tract infections and nephritis in children with bronchiectasis probably contraindicates such a procedure in severe weather. Arrangements for school work should be made for all except the acutely ill child as treatment will be for a long period.

As distinct from treatment of the prebronchiectatic state, convalescent care is of less value in treatment of established bronchiectasis. The improvement observed during convalescence is frequently of a temporary nature only, regression of symptoms occurring on return to home surroundings, and it hardly seems justifiable to keep such a child away from home life. But convalescence is of value for the child with bronchiectasis whose condition is deteriorating and for the child who is undergoing a period of observation before a decision to operate is taken. It is also helpful for short periods before and after operation.

In my opinion, climatic conditions are important for the child with bronchiectasis. During a special follow-up of cases, practically every child reported exacerbation of symptoms—almost to the day—at the onset of the fogs. One of our patients is at school in Switzerland and while there loses her cough, but it returns every time she comes back to England. Again, the majority of our cases convalesce either at Meath Hospital School in Surrey, a special open air school for bronchiectatic children, or at St. Catherine's Home, Ventnor, Isle of Wight. Meath School is situated in country low-lying and damp. St. Catherine's Home is high and dry on a small slope facing the sea. Although the care in both Homes is equally good it is the impression of the author that the children at St. Catherine's Home make better progress than those at Meath Hospital School and climatic conditions may account for this.

It is advisable to have facilities for treating chronic nasopharyngeal infection and

sinusitis while the child is carrying out the medical régime. For this a neighbouring hospital is advantageous.

Chemotherapy.—Expectorants are rarely if ever needed. The cough is present for a purpose, to rid the child of secretions, and is rather to be encouraged than depressed so that depressant cough medicines play little part in medical treatment. But with the introduction of sulphonamides, penicillin and streptomycin, a new field of therapy has been opened. So far it has been disappointing for the chronic cases because after a period of improvement, drug resistant organisms tend to multiply and the patient's condition reverts to its previous state. However the combined use of penicillin and streptomycin may offer better results. Siltzbach,[9] using penicillin, found intratracheal injections most effective but this treatment was only recommended before operation. Dormer and Wiles[10] used a mixture of penicillin and sulphanilamide for intratracheal injection. They reported better results than with penicillin alone. Some lasting effect, however, was obtained with nebulised penicillin. Olsen[11] obtained considerable reduction in sputum with nebulised penicillin if the organisms in the sputum were Gram positive but gained a much better result with an aerosol mixture of penicillin and streptomycin.

A number of the cases in this study were treated for long periods of time with nebulised penicillin without any lasting effect.

Régime for Surgical Treatment.—This does not differ from the medical treatment just described except for the immediate pre- and postoperative procedure.

Preoperative.—About two to three weeks before the operation, more attention is paid to careful postural drainage and physiotherapy with chest clappings. If not already instituted, localised respiratory movements over the area of lung to be removed should be encouraged so that after the operation expansion of the remaining pulmonary segments will be facilitated and deformities of the chest less likely to develop. Children can be taught to move any one part of their chest more than another and once having learned the technic it is not readily forgotten. It is often necessary to admit the child to hospital for a few weeks prior to operation in order to carry out the above procedure.

Children who are coughing up a great deal of purulent sputum frequently benefit from daily intratracheal instillation of penicillin if the organisms in the sputum are penicillin sensitive. It is given in doses of 50,000 units daily for one or two weeks before operation so that the optimum effect will be reached at operation. Siltzbach[9] considers it is the most effective way of reducing the sputum, recording a 50% or more reduction. Possibly better results will be obtained with a combination of penicillin and streptomycin.

Postoperative.—As soon as the child is sufficiently conscious, coughing up of sputum is encouraged to clear the airway to ensure re-expansion of the retained lung. Recently, to facilitate this procedure, some patients have been placed in a steam tent on return to the ward to loosen bronchial secretions. Breathing exercises are recommended as soon as possible after operation, usually by the second day, gently at first but gradually increasing the amplitude until the child is up and about and able to join in the general classes. As a rule, this stage is reached by the third week. Postural drainage is not usually reinstituted until the child's condition has improved, that is, generally about the fifth or sixth day. In most cases it is an advantage to arrange a period of convalescence for two months or more to encourage full expansion of the remaining lung.

Surgical Procedure.—The technic used by the Surgical Unit at University College Hospital, London, on the cases recorded here has been the method of dissection lobectomy, pneumonectomy, or segmental resection. Preliminary results were recorded by Pilcher[7, 12] in 1944 and in 1946 he discussed the method of segmental resection.

Ancillary Methods of Treatment.—Wishart[13] found that repeated bronchoscopic aspiration gave symptomatic relief. Churchill[14] (1937) agreed that there was a reduction of sputum and foul odour to the breath, but considered the results no better than those produced by postural drainage. In children the procedure is not without danger and is not recommended. Hennell[15] advocates treatment by artificial pneumothorax. It may occasionally produce improvement in symptoms, but only of a temporary nature. Preoperative phrenic evulsion produces no improvement and will delay full postoperative expansion of the lung. Mediastinal shift after lobectomy or pneumonectomy rarely causes distress in children. Postural defects are easily corrected, and pathologic emphysema of the opposite lung a less disturbing factor than in adults. Riggins[16] had no success with autogenous vaccines and considers roentgen therapy to be contraindicated in view of the danger of producing further "pneumonitis" and irreversible fibrosis.

Prognosis

It is necessary to complete a long term follow-up of cases for an accurate assessment of progress and comparison of medical and surgical treatment of bronchiectasis. At the time of writing 223 cases are under observation. Twenty-one of these have been excluded from this report because the duration of follow-up has been inadequate or surgical intervention too recent to assess progress. Of the remaining 202, all medical cases have been followed for at least three years, some for as long as 10 years, and most surgical cases have been under observation for three years or more, but as operative removal of the diseased part is incomplete in a number of these, the figures have been separately tabulated to explain the clinical results (Chart 1). It will therefore be appreciated that the following records give an incomplete picture of the ultimate prognosis in children with bronchiectasis and this communication is essentially a preliminary report.

Clinical progress was assessed by noting the severity of the cough, the quantity of sputum, the gain in weight and height, the activity of the child and general demeanour. It is a personal assessment and therefore open to criticism. However, no case was classified as cured unless the child had no cough both by history and personal observation, and no adventitious sounds in the chest. Clubbing sometimes disappeared in medically treated cases and usually following removal of the diseased parts, but chronic chest deformities tended to persist.

From Table I and Chart 1 it will be observed that 13 cases treated medically lost all their signs and symptoms including 5 with asthmatic symptoms. Of these 13 cases one has shown so far a gradual reduction in the degree of dilatation as observed in four repeat bronchograms extending over four years until the last picture of the bronchial tree would almost pass as normal. Four were examples of varicose bronchiectasis and two of cystic bronchiectasis of the right upper lobe. Six cases gave a history of one year's duration or less when first seen; in no case was the dilatation of the bronchi severe or getting worse and in some it appeared to be improving.

Both medical and surgical cases were complicated by asthma. When this was the case, it frequently prevented the child's being classified as cured although symptoms were absent between the attacks. However, it will be noted in Table I that when radical removal of the diseased part was completed a high percentage (54%) were classified as

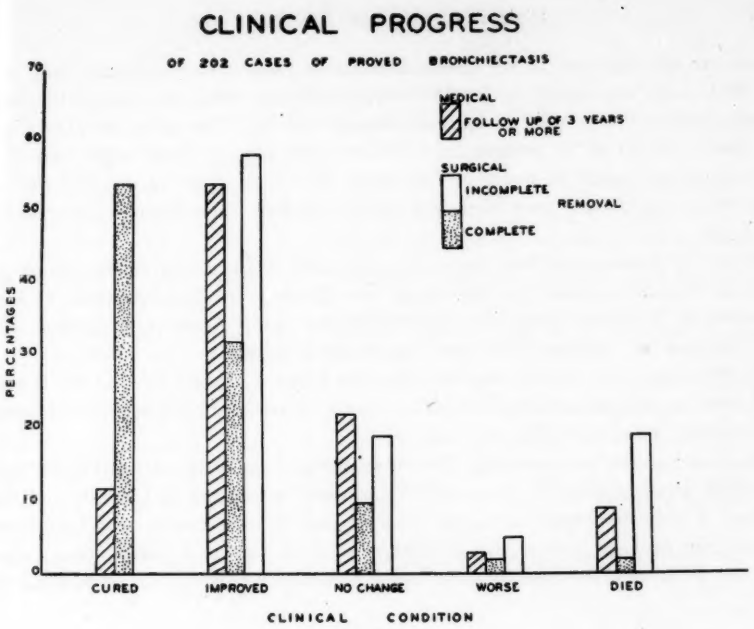


CHART 1

TABLE I FOR CHART 1

CLINICAL PROGRESS IN 202 CHILDREN WITH ESTABLISHED BRONCHIECTASIS

			Cured		Improved		Stationary		Worse		Died		Total	
			No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Medical		No Asthma	8	13	35	57	8	13	1	1.6	9	15	61	100
		With Asthma	5	10	24	50	16	33	2	4	1	2	48	100
Surgical	Complete Removal	No Asthma	26	68	9	23	3	8	0		0		38	100
		With Asthma	1	8	7	58	2	17	1	8	1	8	12	100
	Incomplete Removal	No Asthma	0		13	54	5	21	2	8	4	17	24	100
		With Asthma	0		12	63	3	16	0		4	21	19	100
		Total	40	20	100	50	37	18	6	3	19	9	202	100
							Total Percentages							
Medical			12		54		22		3		9		100	
Surgical	Complete Removal		54		32		10		2		2		100	
	Incomplete Removal		0		58		19		5		19		100	

cured. At the other end of the chart, although 10 cases treated medically died, in nine of these death was caused by the fulminating infection which had caused the bronchiectasis. Eight of these were in the first two years of life. This early mortality is shown in Moll's series[17] of 55 autopsy cases. Of the nine surgical deaths eight were the immediate or late result of operation; however, five of the latter occurred in the earlier years before satisfactory team work had been established. Table II summarizes the causes of death.

Table III demonstrates that disease on both sides is not a contraindication to operation as 10 cases operated on both lungs are classified as clinically cured. This table, however, is deceptive unless it is remembered that many of the cases operated on one side only may have disease in the other lung awaiting removal.

Progress was also assessed anatomically (see Chart 2, Tables IV and V) according to pulmonary segments to find out if the disease in any particular segment deteriorated or recovered more frequently than another.

As bronchograms are sometimes difficult to interpret and frequently fail to fill in some segments, any assessment of facts will be open to criticism but in Charts 2 and Tables IV and V only those branches in the bronchograms that are easy to read have been included. For progress at least two bronchograms must have been performed on the one side but in many cases three or more repeat bronchograms have been done. Since num-

TABLE II

CAUSES OF DEATH

A. *Medically Treated Cases*

Age in years	Autopsy Findings
1, 9/12	Bilateral bronchopneumonia, with areas of collapse and emphysema and some dilatation of bronchi. Duodenal ulcer.
11/12	Bronchopneumonia with collapse and emphysema and early bronchiectasis. Recent alveolar haemorrhages and other signs of scurvy.
2/12	Confluent bronchopneumonia. Bronchiectasis in both upper lobes and left lower lobe. Early left emphysema.
11/12	Bronchopneumonia left lower lobe. Diffuse purulent bronchitis with collapse and emphysema. Bronchiectasis right middle lobe.
5/12	Areas of bronchopneumonia with dilated bronchi. Diffuse purulent bronchitis with emphysema. Collapse left lower lobe with bronchiectasis.
10/12	Diffuse bronchopneumonia both lungs. Collapse part of right upper lobe with bronchiectasis. Gastroenteritis and haemorrhages.
6/12	Scattered areas of consolidation, collapse and emphysema with some bronchial dilatation.
9/12	Polypi of larynx and vocal cords with oedema. Bilateral diffuse pulmonary collapse with saccular bronchiectasis in lower lobes.
6, 2/12	Pulmonary abscess left lower lobe. Localised empyema left base. Bilateral basal bronchiectasis.
7	Tuberculous nodular granulations of larynx and vocal cords. Collapse right middle lobe with bronchiectasis. Old healed tuberculous lesion in lingula lobe.

TABLE II (Continued)
CAUSES OF DEATH

B. *Surgical Cases*

Age	Extent of disease	Previous operative removal	Time of death in relation to operation	Autopsy finding
$4\frac{7}{12}$	RLL, LLL	None	During RLL Lobectomy.	Cause of death not determined.
$7\frac{3}{12}$	RML	None	During RML Lobectomy.	Cause of death not determined.
$10\frac{8}{12}$	RML, RLL LLL and Ling. Post-operative LUL	RML LLL and Ling. LUL	At end of operation for closure of persistent sinus left chest.	Cause of death not determined. Slight amyloid change in spleen.
$10\frac{5}{12}$	LLL	None	At end of LLL Lobectomy.	Signs of shock.
$9\frac{1}{12}$	RML, RLL	None	One day after RML and RLL Lobectomy.	Asphyxia from blood stained mucopus in bronchial tree. RUL collapsed. Left lung emphysematous.
$6\frac{9}{12}$	RML, RLL LLL	LLL No sign of tuberculosis at this operation. Mantoux neg.	One day after RML and RLL Lobectomy.	Congestion and oedema of both upper lobes. Miliary tuberculosis L. lung. Fibrous tuberculous pleurisy right lung with sub-pleural focus.
$8\frac{7}{12}$	RML, part RLL; LLL and Ling.	RML, Cardiac and post basic (Right)	$1\frac{1}{2}$ days after partial resection LLL and Lingula lobectomy.	Pulmonary oedema. Aspiration of vomitus. (Rheumatic) endocarditis mitral valves.
$7\frac{4}{12}$	RML, RLL from TB Hilar gland.	None	$2\frac{1}{2}$ days after RML and RLL Lobectomy.	RUL collapsed. Pulmonary oedema of left lung with fibrous pleurisy. (Rheumatic) endocarditis of mitral valve.
$8\frac{3}{12}$	RLL, LLL and Ling.	RLL LLL	$4\frac{7}{12}$ yrs. after last operation.	No post mortem. Clinically she died of cardiac failure from severe asthma and emphysema.

bers involved are small no firm conclusions can be reached but the figures suggest that there is a greater tendency for the dilatation to get worse or remain stationary rather than improve, and an even greater tendency for the pectoral (antero-lateral) branches of the right upper lobe to deteriorate (Figs. 6 and 7, Part II). The left lower and lingula tend to remain stationary but the apical branches of the right upper lobe and the dorsal

TABLE III

CLINICAL PROGRESS ACCORDING TO EXTENT OF OPERATION

Extent of Operation	Cured	Improved	Stationary	Worse	Died	Total
Unilateral	17	25	8	2	5	57
Bilateral	10	16	5	1	4	36

branches of the left lower lobe show a greater tendency to improve. On the left side postoperative collapse of the left upper lobe leading to bronchiectasis accounts for the high number showing deterioration (see Figs. 8 and 9). These observations may be helpful when considering surgical removal of segments.

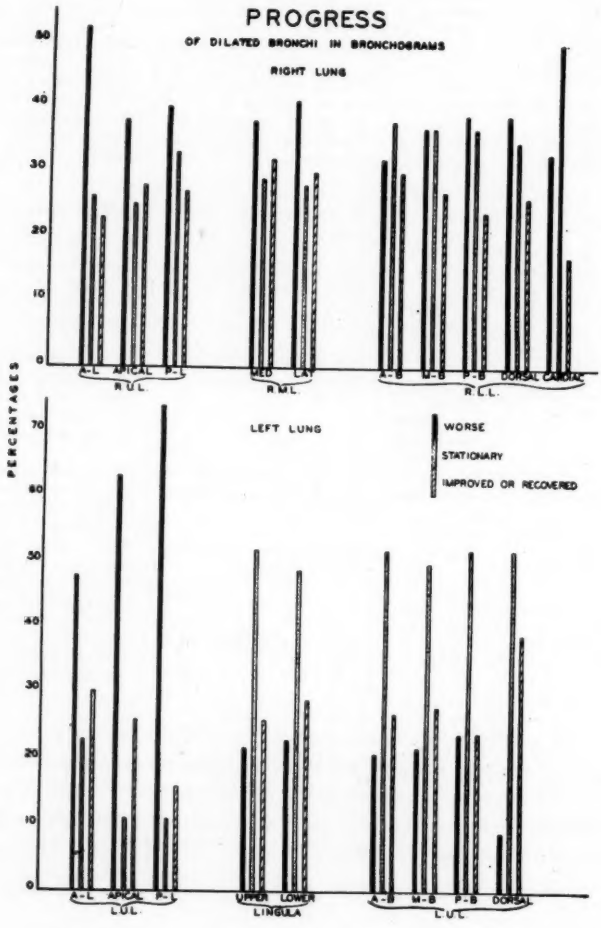


CHART 2*

To assess the prognosis according to the type of bronchiectasis is a more difficult procedure and at present only a general impression resulting from a close clinical and bronchographic study can be given.

Varicose bronchiectasis with its characteristic beading of the bronchi was commonly

* LUL (lower right hand corner) should read LLL.

TABLE IV FOR CHART 2

PROGRESS ACCORDING TO BRONCHOGRAPHIC PICTURE

		Worse			Stationary	Improved and Recovered	Improved	Recovered
		Medical Cases Before Operation	After Operation	Total	Total	Total		
Right Upper Lobe	Ant-lat. (Pectoral)	11	5	16	8	7	5	2
	Apical	3	3	6	4	6	4	2
	Post-lat. (Subapical)	4	2	6	5	4	3	1
Right Middle Lobe	Med.	18	2	20	15	17	13	4
	Lat.	20	2	22	15	17	13	4
Right Lower Lobe	Ant-basic	7	5	12	14	11	10	1
	Mid-basic	5	10	15	15	11	11	—
	Post-basic	8	10	18	17	11	11	—
	Dorsal	5	4	9	8	6	5	1
	Cardiac	2	2	4	6	2	2	—
Left Upper Lobe	Ant-lat. (Pectoral)	5	10	15	7	9	8	1
	Apical	4	8	12	2	5	2	3
	Post-lat. (Subapical)	5	9	14	2	3	2	1
Lingula	Upper	10	1	11	26	13	10	3
	Lower	12	—	12	26	15	10	5
Left Lower Lobe	Ant-basic	13	—	13	32	17	14	3
	Mid-basic	15	—	15	34	19	14	5
	Post-basic	16	—	16	35	16	13	3
	Dorsal	3	—	3	17	13	10	3
	Cardiac	—	—	—	1	—	—	—

observed. It produced few symptoms and usually clinical progress was good and the child sometimes lost all symptoms and signs (see Fig. 10).

Fusiform bronchiectasis with its dilated mid-portion and tapering periphery was not common. It is suggested that this type of bronchiectasis may be caused by the opening up of some of the collapsed alveoli but not all so that the periphery of the bronchus continues to grow on a smaller scale (see Fig. 11). The children with this type of bronchiectasis usually did fairly well clinically and the dilatation tended to improve over the years.

Tubular bronchiectasis can be divided into two types for the purpose of prognosis. If the bronchus was pipestem and of equal diameter along its length then this was

TABLE V FOR CHART 2

PROGRESS ACCORDING TO BRONCHOGRAPHIC PICTURE IN PERCENTAGE OF TOTAL

		Worse	Stationary	Improved and Recovered
Right Upper Lobe	Ant-lat. (Pectoral)	52	26	23
	Apical	38	25	28
	Post-lat. (Subapical)	40	33	27
Right Middle Lobe	Med.	38	29	32
	Lat.	41	28	30
Right Lower Lobe	Ant-basic	32	38	30
	Mid-basic	37	37	27
	Post-basic	39	37	24
	Dorsal	39	35	26
	Cardiac	33	50	17
Left Upper Lobe	Ant-lat. (Pectoral)	48	23	30
	Apical	63	11	26
	Post-lat. (Subapical)	74	11	16
Lingula	Upper	22	52	26
	Lower	23	49	29
Left Lower Lobe	Ant-basic	21	52	27
	Mid-basic	22	50	28
	Post-basic	24	52	24
	Dorsal	9	52	39

FIGS. 8 and 9. Effect of natural drainage on development of bronchiectasis.

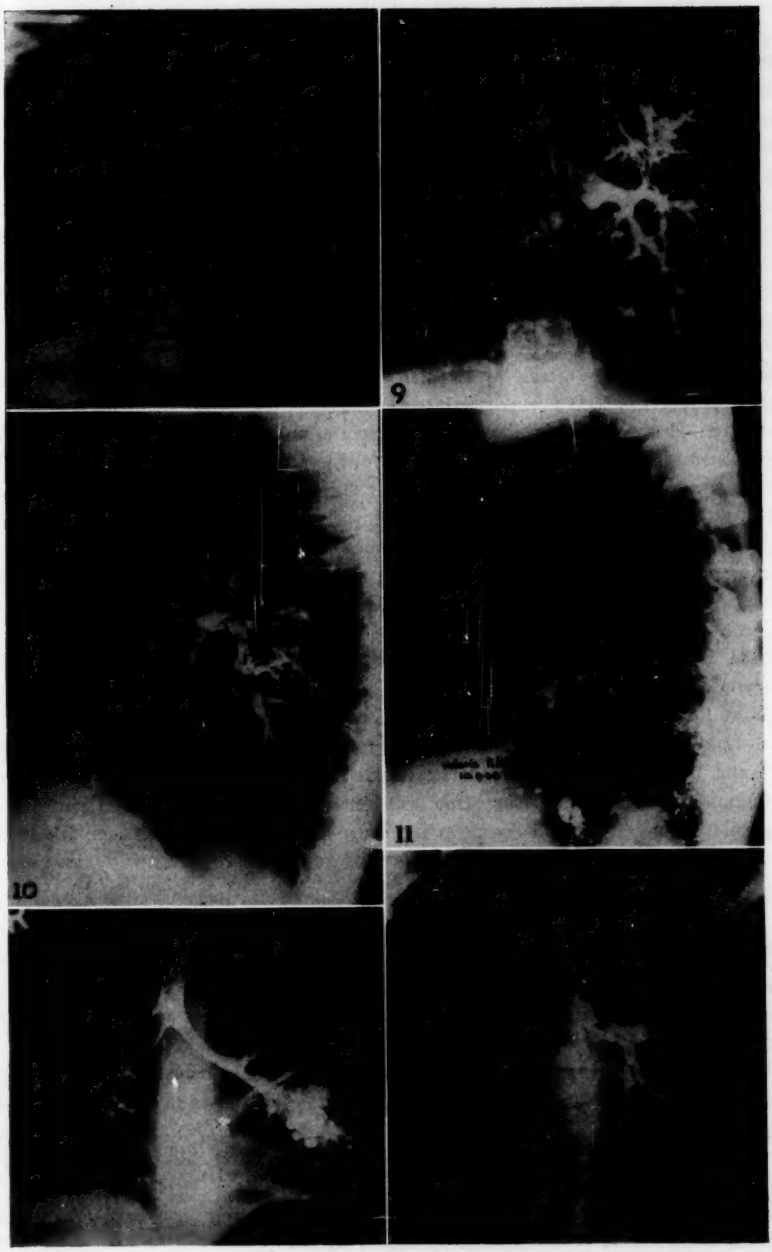
FIG. 8. Left A-P bronchogram from girl 4 mos. after left lower and lingula lobectomy. Incomplete expansion of LUL has produced slight generalised bronchial dilatation. Fig. 9. 10 mos. later. Dependent branches whose secretions drain against gravity have become irreversibly bronchiectatic; bronchi directed toward apex whose drainage of secretions are assisted by gravity have reverted to normal calibre.

Fig. 10. Left oblique bronchogram from boy aged 11 yrs. showing generalised varicose bronchiectasis. He gradually lost all symptoms and signs but repeat bronchogram 5 yrs. later showed little change in bronchiectasis. Fig. 11. Left lateral bronchogram showing fusiform bronchiectasis of posterior basic branch. It is suggested that this type of bronchiectasis is result of partial re-expansion of collapsed area so that bronchus continues to grow as narrower tube as seen in picture.

FIGS. 12 and 13 demonstrate growth of bronchi in remaining lung after lobectomy.

FIG. 12. Left A-P bronchogram showing incompletely filled cystic dilatations in LLL (probably congenital). Fig. 13. 2 yrs. after left lower lobectomy. Lingula is now occupying lower lobe area and has grown in length curving along diaphragm to costophrenic angle.

sometimes merely the effect of pulmonary collapse which reversed to normal calibre when the segment re-expanded. This type of bronchiectasis was kept under observation for at least a year. Bronchi that showed a greater dilatation of the bronchus at the periphery



FIGS. 8-13. See opposite page for description.

than near the main stem (club-shaped) usually remained permanently dilated and tended to get worse so that lobectomy was usually recommended (Figs. 5 to 7).

Saccular (cystic) dilatation was usually permanent, and produced symptoms and signs according to the degree of infection. In some cases (probably congenital in origin) few symptoms were produced particularly if the diseased area was in the upper lobe, and in these it hardly seems justifiable to recommend lobectomy (Fig. 3, Part II). But where purulent infection was present some most dramatic recoveries were seen following surgical removal.

Regeneration of Lung.—In the growing child after surgical removal of parts of a lung it is a well observed fact that the remaining bronchi grow in length and the remaining pulmonary tissue itself may come to occupy almost the same area as the original whole lung (Figs. 12 and 13). Exactly what happens to the alveoli is still under dispute; whether new alveoli are formed as described in kittens by Bremer[18] or whether the pulmonary expansion is the result merely of alveolar distension with increased vascular and interalveolar tissue as observed in young rats (Field, to be published) remains to be proved in children. However, the child's functional capacity after lobectomy and pneumonectomy improves and becomes higher than predicted for the remaining lung (Cournand et al.[19]). This compensatory mechanism is much greater during the growing period, a fact that has been demonstrated in puppies when compared with dogs (Longacre and Johansmann[20]).

In this series of bronchiectatic children, lobectomy or pneumonectomy seems to cause little or no ultimate clinical respiratory limitations. The children take part in all school activities without complaints. In the few cases where more than half the pulmonary tissue has been removed, there seems to be a tendency for dyspnoea to occur more easily on exercise. It is therefore recommended that as much good lung as possible be retained at operation, segmental resections being performed where indicated.

Future Outlook.—In the second decade it has been shown that there is a tendency for the symptoms resulting from bronchiectasis to improve. But what will happen in the third and fourth decades? With the stresses and strains of adult life, will the patient's condition deteriorate and the bronchiectasis get worse? Or will the good parts of the lung enlarge and grow, and compress the diseased parts into a small area where they can cause little disturbance? Only a prolonged follow-up of cases will answer these questions.

Summary

Prevention of bronchiectasis means prevention or better treatment of the predisposing conditions, particularly pneumonia, pertussis, pulmonary collapse and so-called "chronic bronchitis." When the cough persists after one of these conditions adequate convalescent care coupled with postural drainage and breathing exercises is advocated.

Once bronchial dilatation is considered irreversible, the treatment offered can be surgical or curative, medical or palliative, or partial surgical removal to alleviate the symptoms.

In general radical surgical treatment is recommended in all cases where an adequate amount of healthy lung can be preserved.

Medical treatment can be carried out at home, at an open air school or at a convalescent home. It includes postural drainage, breathing exercises and general health measures.

Chemotherapy for established bronchiectasis has so far been disappointing. Aerosol

penicillin in a number of cases produced no lasting effect but more promising results have been reported with combined penicillin and streptomycin.

Two hundred and two cases of proved bronchiectasis have been followed for varying periods up to 10 years. Although fewer cases were treated surgically, twice as many were classified as cured compared with the medically treated cases. However, 13 of the latter lost all signs and symptoms. Out of 19 deaths, 9 had been treated surgically.

Ten cases classified as cured had bilateral lobectomy.

Serial bronchograms taken over the years revealed the frequent deterioration or increase of dilatation in the antero-lateral (pectoral) branches of the upper lobes in contrast to the improvement or cure of the apical branches.

Varicose and fusiform types of bronchiectasis produce the least physical disturbance.

Although the clinical progress of established cases of bronchiectasis showed improvement in the majority of cases in the first two decades, it is feared that deterioration may occur in the third and fourth decades.

The fact that after lobectomy the remaining lung increases its functional capacity in growing children makes it desirable to operate during childhood.

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SPANISH ABSTRACT

Bronquiectasia en la Niñez. III. Profilaxis, Tratamiento y Progreso con un Estudio Perseguido de 202 Casos de Bronquiectasia Establecidos

La prevención de la bronquiectasia significa prevenció o mejor tratamiento de las condiciones predisponentes. Una vez que la dilatación bronquial sea irreversible, el tratamiento puede ser quirúrgico o médico. Se recomienda el tratamiento quirúrgico cuando se puede preservar una cantidad adecuada del pulmón sano. El tratamiento médico incluye drenaje postural, ejercicios de respiración y medidas de salud en general.

La quimioterapia no ha sido satisfactoria. La penicilina Aerosol no produjo efectos duraderos en un número de casos, pero se han reportado resultados que prometen con penicilina y estreptomicina combinadas.

Se han seguido 202 casos de bronquiectasia probada en diez años. Los casos quirúrgicos clasificados como curados fueron dos veces más que los casos médicos. Sin embargo, 13 de los últimos perdieron todos los signos y síntomas. De 19 muertes, nueve fueron tratadas quirúrgicamente. Once casos clasificados como curados recibieron lobectomía bilateral.

Una serie de bronquiogramas reveló frecuente deterioración en las ramas antero-laterales de los lóbulos superiores en contraste con la mejoría de cura de las ramas apicales.

Tipos varicosos y fusiformes de bronquiectasia produjeron el menos desorden físico.

Aunque el progreso de los casos de bronquiectasia mostraron mejoría en la mayoría de casos en las dos primeras décadas, pueda ser que en la 3ra. y 4a. décadas haya deterioración.

El hecho de que el pulmón que queda aumenta su capacidad de funcionamiento después de la obectomía en niños que crecen hace conveniente la operación durante la niñez.

Great Ormond Street

Pediatrics

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SPECIAL SECTIONS

THE PEDIATRICIAN AND THE PUBLIC

AN OPEN FORUM

PAUL A. HARPER, M.D., *Editor*

Statements appearing in this column do not necessarily reflect the opinion of the editors nor are they to be interpreted as the official opinion of the Academy.

INTRODUCTION

THE two communications in this issue are from Dr. George Baehr, President of the New York Academy of Medicine, an organization which has a long tradition of study of the problems of medical care. First is the statement made in behalf of this Academy before the Senate Committee which has been hearing testimony concerned with the various medical care bills now before Congress. This statement is a succinct and thoughtful appraisal of these bills and indicates that S-1970 (Flanders-Ives-Herter-Javits Bill) comes nearest to meeting the Academy's requirements for a voluntary prepaid comprehensive medical service plan.

The second communication is Dr. Baehr's analysis and comments upon S-1970 (Flanders-Ives-Herter-Javits Bill). He points out that, in the words of Senator Flanders, S-1970 is essentially a " 'voluntary health insurance bill calling for compulsory public contribution,' " which is to take the form of a subsidy for the operating deficits of voluntary prepayment agencies. Other outstanding features of the bill are the provisions designed to stimulate group practice and the requirement that subscription charges shall vary with income.

The implications of a subsidy for the operating deficits of voluntary agencies and the fostering of group practice on a nation-wide scale will warrant careful study. It should also be noted that individuals with wide experience in existing prepayment organizations have expressed real concern as to the feasibility of private organizations doing business with clients on a sliding premium basis. These three provisions have added important considerations for those concerned with the development of sound legislation.

Statement by Dr. George Baehr on Behalf of The New York Academy of Medicine, Made at the Public Hearings Before the Senate Committee on Education and Public Welfare, on June 20, 1949

Dr. Howard Craig and I are pleased with this opportunity to appear before you at the

invitation of your Chairman to testify on behalf of the New York Academy of Medicine. To save time, we refer you to the statements and testimony which I gave as President of the Academy at previous hearings before this Committee on May 24, 1946 (pp. 2060 to 2079) and on May 22, 1947 (pp. 121 to 164). For the benefit of those Senators who were not members of this Senate Committee in those years, I should like to give a condensed version of that testimony as a brief preamble to comments on the health bills before the 81st Congress.

The membership of the Academy consists of about 2,500 Fellows and Associate Fellows, among whom are many of the most distinguished practicing physicians, specialists, medical educators and medical scientists, not only from the New York area but from many parts of the country. Its primary purposes are the promotion of public health, the extension of medical education, the advancement of the medical sciences and the improvement of medical practice. In line with these purposes, it maintains one of the great medical libraries of the world, to which the general public and the entire medical profession have free access.

It has been our desire, like yours, to find the best means of bringing the modern benefits of preventive and curative medicine to all the people of our country, rural and urban. We are not interested in maintaining the "status quo" and are prepared to consider any changes in the methods of rendering medical services and of payment for medical care which may be better for the people. Accordingly, a special Academy Committee on Medicine and the Changing Order recently completed an intensive four year study, the factual material of which has been assembled in 11 monographs published by the Commonwealth Fund. A 12th volume, entitled *Medicine in the Changing Order,* contains the summary report and the Academy's findings and recommendations.

In brief, I should like to state that the Academy is fully cognizant of the many lacks in medical care which now exist throughout the United States. We are in complete agreement on the principle that the health of the people is a matter of national concern and that every effort should be made to provide all our people with adequate medical care. From our experience and our study of the problem, we feel certain that National Compulsory Medical Insurance as proposed in the Thomas bill, S. 1679, would result in most detrimental changes in medical practice and would harm the public. We are also convinced that the objectives which the proponents of this bill have in mind, and which we share, can be achieved more effectively by procedures which are more orderly, progressive and far less hazardous.

National Compulsory Medical Insurance would indeed provide the funds with which to pay for medical care wherever it is available. Probably 80,000,000 people or more would pay in advance through payroll deductions or other contributory methods for home and office care, laboratory, diagnostic and consulting services, and specialists' services outside and within hospitals. Yet, in many parts of our country, either such services are unavailable or only an inadequate fragment can at present be obtained. Our government cannot collect the money in advance and not be prepared to "deliver the goods" promptly on demand.

These deficiencies in the availability of adequate medical care are now recognized realistically in S. 1679 as they are in the other omnibus health bills before the Congress. Provision is therefore made in other titles of this and other bills for aid to medical, dental and nursing education; for encouragement of a better distribution of medical services, especially in rural areas; for a more rapid construction of physical facilities, etc.

However, it may take a generation of consistent effort by federal, state and local authorities before the required amount of medical personnel and physical facilities can be developed, which would permit our government and private agencies to fulfill their joint obligation to the people if nation-wide compulsory medical insurance were enacted.

In regard to the gross inequalities among the states in just one branch of medical practice, I invite your attention to the recent report of the American Academy of Pediatrics on Child Health Services and Pediatric Education, published by the Commonwealth Fund. It should be obvious that we in this country, with our 48 very different states and their inequalities, are far from being ready for such a momentous step.

A second fundamental fault which the proponents of compulsory medical insurance have not faced is that the method of remunerating physicians by the payment of a fee for each service, a method which almost the entire profession of this country will choose because it is more profitable, will result in a gigantic, nation-wide "medical racket" involving patients and doctors alike. Under a "fee-for-service" system of payment by an insurance fund, the pressure of subscribers for services and the financial rewards to the physician for mere volume of services constitute a combination of influences difficult to resist. The inevitable result is superficial performance and a disastrous deterioration in the standards and ideals of medical practice throughout the nation.

The alternative method of payment proposed in S. 1679, namely, capitation, whereby an annual payment is made to the physician for each insured patient on his panel, would be acceptable in this country only to some medical practice groups. It is quite obvious to those who know something about medical administration under existing prepayment plans that significant changes must occur in the organization of medical practice and in the methods of payment before comprehensive medical services, preventive and curative, can be provided to persons who prepay their medical needs under any insurance plan, compulsory or voluntary. S. 1679 fails to provide financial or other material encouragement to physicians to organize themselves into medical group practice units. The Humphries bill (S. 1805) wisely recognizes this need but limits assistance to medical groups which are part of cooperatives. Its provisions should be extended to medical practice groups serving nonprofit medical insurance plans which may not be cooperatives.

The Academy has proposed a much better and far less hazardous alternative to national compulsory insurance, which would permit us to build upon the excellent structure of American medicine and extend it progressively and as rapidly as possible to all the people of this country. At the hearings of this Senate Committee in 1946 and 1947, we urged the enactment of legislation to provide federal grants-in-aid to the states for the study of state and local needs and the development of state and local programs designed to correct these deficiencies in accordance with acceptable federal standards. In this country, the provision of medical care has been and will always continue to be a local responsibility except for such conditions as mental disorders, tuberculosis and chronic illnesses which require prolonged hospitalization and must largely be a responsibility of the state. In every locality in which medical personnel and facilities are seriously deficient, the reasons are ignorance, lack of financial resources or geography. It should be the responsibility of government to aid in correcting the major existing deficiencies by providing sufficient state and federal assistance to raise local medical resources to a desirable level. Entirely different procedures will be required in some rural areas from those in urban centers and not all urban communities need identical treatment.

In order to encourage the people to contribute as adequately as possible to the support

of their own local medical services and facilities, federal and state aid will be required to assist them in establishing and maintaining local, regional or state-wide prepayment plans for medical care. The Academy is opposed to S. 1679 with its program of national compulsory medical insurance because it involves precipitate changes in medical practice of nation-wide scope which would be irreversible. It would not be averse to experimentation with such a procedure over a limited geographic area. The Academy prefers voluntary nonprofit medical insurance plans because they are flexible and permit local initiative and experimentation. Such plans cannot be designed primarily for the indigent or medically indigent, but are required for people with moderate incomes. The contributory premiums for families on relief should be paid by government, for those temporarily unemployed, by the unemployment insurance funds, as in the Hill bill (S. 1456). The contributions by persons gainfully employed should be proportional to their earnings up to a definite income ceiling, as in the Flanders-Ives bill (S. 1970), so that the lowest income group can afford to subscribe.

It is important that the federal and state governments contribute a fraction of the total operational cost out of general tax funds as grants-in-aid and that premium payments be deductible on income tax returns, so that there will be a compelling incentive for all people to subscribe to the plans. This would also provide the necessary financial stability to the plans during periods of business recession when wage levels fall and premium income is reduced.

The Academy is also convinced that it is essential that such prepayment plans should meet the following requirements:

1. They should maintain the professional and operational standards required by federal and state health councils;

2. They should provide financial and other incentives to physicians which will encourage them to organize themselves into medical practice groups. Such medical groups can provide comprehensive medical care, preventive as well as curative, and can effectively render such services to subscribers in return for capitation payments. Medical practice groups can also serve as the yardstick with which to measure the performance of "solo" practitioners and specialists remunerated on a fee-for-service or capitation basis;

3. They should provide similar incentives to the staffs of teaching hospitals and to other approved hospitals and health centers to organize themselves into units for medical group practice related to the general physicians in adjacent urban and rural areas. In this manner young physicians will learn to appreciate the financial, professional and educational advantages of group practice, to the end that the practice of medicine may be gradually transformed in future years, at least in part, to a form which can maintain high standards of professional service and be capable of functioning more efficiently and economically under prepayment plans than under the present method of "solo" practice. In this manner evolutionary changes in medical practice can be initiated without any sudden and violent dislocation of the medical profession or a lowering of medical standards and ideals;

4. They should develop a regional interrelationship of medical centers and teaching hospitals to smaller institutions, local health centers and even individual physicians in outlying communities.

For the reasons stated, the Academy wishes to record its disapproval of S. 1679 (Thomas bill). It approves in principle S. 1456 (Hill bill), S. 1581 (Taft-Smith-

Donnell bill), S. 1805 (Humphries bill) and S. 1970 (Flanders-Ives bill), with reservations in regard to details in all these bills.

S. 1456 and S. 1581 are based too heavily upon a program designed primarily for the indigent and medically indigent. A medical care plan must provide for the needs of all people of moderate income and, of course, include the indigent in these benefits. A means test for eligibility to a prepayment plan is impractical and undesirable if the plan is ultimately intended to include a major part of the total population.

S. 1456 fails to make any provision for comprehensive medical services to subscribers. Prepayment for medical care of conditions which require hospitalization or other limited medical benefits are desirable as incentives to thrift but they have no significant influence upon the extension of medical care or upon the quality of medical services. Such limited benefit plans certainly play no role whatever in preventive medicine and have little influence upon encouraging prompt and early recognition of disease. Yet this is rapidly becoming a matter of urgency in view of our aging population and the increasing number of diseases which can be cured or arrested when detected in an early stage. We therefore recommend that provision be included for comprehensive medical services wherever they can be made available. (The experience of the Health Insurance Plan of Greater New York, which provides complete medical service to its subscribers in return for a premium without any financial or other deterrent, indicates that under these favorable circumstances only 10% of the total medical services are for patients in hospitals and 90% are rendered in physicians' offices, health centers and in the subscribers' homes.)

The development of diagnostic clinics (S. 1456 and S. 1581) as aids to early diagnosis is praiseworthy. I established such a consultation service at the Mount Sinai Hospital, New York, for persons of moderate means almost 20 years ago, which has been in successful operation on an all-inclusive flat-fee basis since that time. In spite of its demonstrated value, I can tell you from my experience that the support of diagnostic clinics by a prepayment plan as an isolated item in medical care is actuarially unsound. Such diagnostic and consulting facilities can be operated under prepaid support only when they are part of a comprehensive medical care plan.

S. 1970 (Flanders-Ives bill) comes nearest to meeting all the Academy's requirements for a voluntary, prepaid, comprehensive medical service plan. There are details in the bill which require amendment, but it contains most of the provisions which we regard as essential for the extension of medical care and the maintenance of high professional standards. Because its program provides for gradual development, it would not suddenly disrupt present methods of medical practice. Through encouragement of medical groups it would tend to improve and gradually transform medical practice by a progressive evolutionary process.

When the Congress enacted the Hospital Survey and Construction Act, those of us who were concerned with problems of medical care were encouraged to believe that the passage of this bill indicated that the Congress had adopted a procedure which it would next apply to the extension of medical care. This would have meant a similar survey of medical care problems by each of the states with the financial and technical assistance of the federal government, for the purpose of uncovering the extent of existing deficiencies and determining the relative priorities for their successive correction. We had hoped that the bill for medical care would contain grant-in-aid provisions similar to those of the Hospital Survey and Construction Act for the correction of the most serious

deficiencies in medical care and that, as with the Hospital Act, a 10 or 20 year program would be adopted which would follow the priorities agreed upon by the state and federal authorities. This seems to be the general philosophy underlying the Flanders-Ives bill (S. 1970) and, to some extent, the Taft-Smith-Donnell bill (S. 1581) and the Hill bill (S. 1456).

In view of the years of debate and endless hearings on this subject, we believe that the time has at last arived for a nonpartisan measure which will accomplish the objectives for which we are striving. A nonpartisan federal commission might be established for this purpose similar to the Hoover Commission or to the Goodenough or Beveridge Commissions in England. The New York Academy of Medicine stands ready to help in any way it can to such an end.

THE FLANDERS-IVES-HERTER-JAVITS BILL

(S. 1970 and HR. 4918-4924)

(Sponsors: Senators Ralph E. Flanders (R.-Vt.) and Irving M. Ives (R.-N.Y.); Representatives Clifford P. Case (R.-N.J.), James G. Fulton (R.-Pa), Robert Hale (R.-Me.), Christian A. Herter (R.-Mass.), Jacob K. Javits (R.-N.Y.), Thruston B. Morton (R.-Ky.), Richard M. Nixon (R.-Calif.), Charles Auchincloss (R.-N.J.).)

Summary of the Bill

The proposed "National Health Act, 1949" is developed within the framework of the Public Health Service Act, (a) adding a new Title VI—which provides an immediate health and medical service program, (b) adding a new Title VIII—which provides for a long-range survey of national health needs, (c) amending existing provisions of Title VI—relating to hospital construction, (d) adding a new provision to Title III—regarding local public health units.

A. The core of Title VII is Part C, providing assistance to voluntary nonprofit prepayment health service plans. These are the salient features:

1. Individuals will obtain medical care for themselves and their families by belonging to and obtaining a medical insurance contract through local "cooperating prepayment health service plans" (which are to be nonprofit organizations, the majority of whose board members must be laymen.) 721(b).

2. These plans must base their subscription charges upon a percentage of the subscriber's net income up to $5,000. 723(n). The Health Region Authority, a lay body appointed by the Governor, determines to what extent the plans are to accept nongroup applicants. No more than 25% of the beneficiaries may reside outside the State. 721(c).

3. The minimum subscription charges will depend upon the benefits provided by a local plan. Section 723(1) sets forth a yardstick of comprehensive medical services, which include home and office care, diagnostic and preventive services, and hospital treatment. For this yardstick, the minimum charge is 3% of the subscriber's income. 723(n). If a plan offers greater, or less, benefits, the minimum subscription charge is adjusted accordingly. 723(m), (n). A plan may offer more than one type of contract.

4. However, it is for the State Health Council to determine, upon the basis of avail-

able personnel and facilities, the maximum range of services and benefits which may be offered by the various plans under the program in that State. 723(i).

5. The Health Region Authority will calculate an "allowed cost," which is its estimate of the normal cost of furnishing the benefits under each approved contract. 723(m). The State will assure each plan that it will recover this "allowed cost," and in the event that subscription income is inadequate, whether due to the low income of the subscribers or their greater health needs, the State will pay the difference. 723(o). An adjustment procedure is provided for plans with adverse "selection factors," e.g., where a disproportionate number of the subscribers are aged. 723(o).

6. The States may make noninterest loans to assist voluntary prepayment plans in their initial establishment. 723(y).

7. The States may make special grants for "special need areas"—defined in 721(i) as regions with not more than eight doctors per 10,000 population—in amounts adequate to assure the personnel and facilities needed to furnish the services set forth in 723(1). 724.

8. As to all these sums paid by the State, the Federal Government will reimburse the State up to its "Federal percentage" of the sum paid. The "Federal percentage" increases as the State's per capita income decreases, but never falls below 33⅓% or exceeds 75%, subject to the qualification that, as to sums paid by the States to participating health service plans to meet their costs, in no event can the Federal reimbursement to the State exceed $15 yearly per beneficiary covered by such plans. 725.

B. Title VII, Part D—Appropriates $10,000,000, so that the Surgeon General may make 4% loans to prepayment health service plans to cover up to 80% of the cost of establishing "personal health service centers" to provide health services to the subscribers and beneficiaries as ambulatory patients. This provision is designed to encourage the establishment of medical practice groups.

C. Title VII, Part E. To alleviate the shortage of doctors and nurses the bill provides:

1. Payments to medical schools of $500 for each enrolled student, plus an additional $1,000 for each enrolled student in excess of average past enrollment. Comparable provisions in lesser amounts are provided for nursing schools. 743.

2. The Surgeon General may grant up to 50% of the costs of construction and equipment of new medical or nursing schools or expansions. 744.

D. Title VIII. Establishes a bipartisan Federal Health Study and Planning Commission —four members appointed by the President; four by the President pro tem of the Senate; four by the Speaker—in each case at least two from private life. 802.

This Commission is to conduct continuing studies of health service needs—obtaining data as to supply and education of qualified personnel; as to health care received within the various regions; as to status of research, health education, hospitals and health centers, etc. The Commission is directed, so far as practicable, to avoid making its own studies but to develop the basic data through contracts with public bodies established by the States and with public and private nonprofit organizations. 805.

The Commission is directed to formulate a 20 year health plan to improve the Nation's health services. This plan is to be submitted to the President and the Congress by January 15, 1953, and is to be revised every two years. The Commission is also directed to make interim reports on certain urgent problems.

For these purposes, up to $5,000,000 per annum is authorized for appropriation.

E. Title VI of the Public Health Service Act—Hospital Construction Program—is amended in certain respects:

1. To permit State grants and Federal contributions for construction of diagnostic centers and personal health service centers, serving ambulatory patients, as well as of hospitals and public health centers. 631.

2. Increases appropriation under the Hospital Survey and Construction Act from $75,000,000 to $175,000,000 per annum, and increases Federal contribution to hospital and other construction projects from a flat 33⅓% to the State's "Federal percentage" (which varies from 33⅓% to 75%). Secs. 621, 624, 625.

3. Provides $2,500,000 per annum for demonstrations to improve the efficiency and utilization of hospitals and health personnel.

F. Title III is amended by inserting sec. 315, relating to local public health units. If a State provides a plan for extending the coverage and services of local public health units, it is entitled to receive a percentage of the cost of the program, the percentage varying inversely with the State's per capita income but not exceeding 66⅔%.

COMMENTS

The preceding summary makes it clear that S. 1970 (which is identical with HR. 4918-4924) is essentially "a voluntary health insurance bill calling for compulsory public contribution," as Senator Flanders recently described it. Although the Hill, Taft and Thomas bills all include provisions for the utilization, in varying degrees, of voluntary plans, S. 1970 is the only one that close analysis shows would actually base a national health program on voluntaries.

The Thomas Bill (successor to the Wagner-Murray-Dingell Bill) merely authorizes the administrators of the national compulsory program to pay what amounts to premiums to privately organized service groups on behalf of people who join such groups; but it is difficult to see why anyone would go to the trouble to set up such plans, or what would lead physicians and hospitals to participate in them, since the services, and direct fee-for-service or other payments for them, would be guaranteed under any circumstances by the Government.

The part that voluntary plans would play under the Taft Bill's program is scarcely more extensive. States could assist such plans out of not more than 25% of the Federal-State funds provided under this bill for medical care, and are authorized to enroll the medically indigent in voluntaries if they consider it practical to do so. But the maximum amount of money called for—$600 million a year—would be insufficient to carry out the primary purpose of the bill (which is to provide within five years complete medical and hospital care to all those "unable to pay the full cost") without confining public aid to outpatient departments, dispensaries and clinics, where the professional staffs would largely donate their services. While $600 million is a large sum, taken by itself, it must be remembered that it represents only 7% of our current annual expenditures for medical care. Thus it seems fair to say that as a practical matter, the Taft Bill pays only token service to the voluntary plans.

The title of the Hill Bill, "The Voluntary Health Insurance Act," makes it appear as a measure designed to enable universal enrollment in voluntary plans. Careful reading of the bill, however, discloses that such is not actually the case. Voluntaries would be utilized only as channels through which public agencies could pay for services rendered

to the medically indigent, after they received them; public funds would not be used to pay premiums in insurance plans for those who could not afford to join them. There are many encouraging words in the bill about voluntary plans, but no substantive action is promised.

In contrast to the largely nominal provisions in those three bills, S. 1970 drives directly at the objective of aiding the voluntaries in such a way as to open them to everyone, irrespective of income. Fundamental to this program is the requirement that voluntary plans base the rate of payment by subscribers upon a percentage of the subscriber's income (up to $5,000). This provision will necessitate changing the flat premium charges employed by most voluntary medical insurance plans at present in existence. It is, however, essential if medical insurance plans are to be brought within reach of people of limited means without resorting to the personally obnoxious and administratively impractical device of the personal "means test."

Because the scaled-to-income subscription charge and the method for determining the amount of public aid going to any plan are basic to the bill, it is worth quoting from an explanation issued by the bill's sponsors.

"In order to participate in the program, a State would set up a State Health Council. This Council would divide the State into several regions, many of which have already been set up under the Federal Hospital Construction Act. Each region would be managed by a Health Region Authority, made up of local people. . . .

"The bill sets up a national yardstick in the form of a comprehensive range of benefits, which it defines in detail and which includes the most vital health services. It further states that the subscription charge for this particular coverage cannot be less than 3% of the subscriber's income up to $5,000. The first duty of each Health Region Authority is to estimate the normal cost in that region of supplying the national 'yardstick' coverage.

"Any plan operating in that region which provides the 'yardstick' range of benefits will receive from the State (with Federal participation) the difference between its subscribers' payments and the estimated normal cost of the coverage.

"A plan may offer a coverage less comprehensive than the national 'yardstick' coverage, in which case it would charge proportionately less to its subscribers and any public contribution would be based on a proportionately lower allowed cost. Or a plan may provide a still more comprehensive coverage, in which case it must charge proportionately more and would have a proportionately higher allowed cost.

"The maximum coverage a plan may offer under the bill's program will be fixed by the State Health Council. This maximum will be based on how much medical service can be provided in each of the State's regions by existing or reasonably obtainable personnel and facilities. The State may amend the maximum each year in the light of experience and in line with the growth of its medical resources.

"Let us suppose that a plan provides the 'yardstick' coverage, for which it charges 3% of each subscriber's income. This would cover the subscriber and any dependents. A subscriber with an income of $1,500 would pay $3.75 a month for complete medical care, preventive and curative, and hospital benefits; one with $2,500 would pay $6.25 a month; and one with $3,800 would pay $9.50 a month. They would all get the same services, the deficit created by the lower incomes being made up by the State-Federal aid. Thus, if the annual cost allowed to the plan by the Regional Authority were $114 per family (which would be about the estimated average for the nation), and if the average

family in the plan paid $75 a year, then the State-Federal aid would contribute $38 per family to cover the deficit to that plan. In the case of unemployed persons or public wards the premiums may be paid by the State, for whatever plan the individual chooses.

"On the basis of these figures it is apparent that a $3,800 family would be paying its full cost. Smaller incomes would be subsidized, partly by the higher-income people who join the plan and partly out of public funds. Partial subsidization of the low-income groups by the higher ones is what happens now, in a rough and unsatisfactory way, through the scaling of charges by the doctors and the hospitals. The highest income used for figuring subscription rates is $5,000. Persons with larger incomes may join the plans and will undoubtedly choose to do so; but many plans may provide that such people be paid fixed sums (called 'indemnity benefits') rather than be covered for the complete cost of their care (called 'service benefits').

"Whether a family decides to come into the most complete plan set up under the State's program in its community, or into a cheaper and less complete plan, or stay out of all of them, is left to its own free choice. Whether a subscriber's employer pays all or part or none of the subscription charge, is for the employer and employee to work out together. Whether a subscriber's contribution is deducted from his pay is also subject to free arrangement. In the case of State and Federal employees, the bill provides that this may be done.

"The basic formula for Federal aid under this bill follows the lines of the Hospital Construction Act. Federal aid will be granted a State in inverse proportion to its per capita income. States having the lowest per capita income will receive Federal aid at a ratio of three Federal dollars for every State dollar devoted to the program; those with the highest per capita income will get one Federal dollar for two State dollars. The average for the nation will be a little more than 50% Federal aid. The ceiling for Federal aid to any given State will be $15 a year for each person covered.

"A State will begin to receive its Federal contribution as soon as it has passed the appropriate legislation and as soon as the machinery is in operation.

"In the sometimes difficult matter of raising money to start a qualified nonprofit plan, the Federal Government will also help the States to help the organizers. Whatever amount the sponsors of a plan can raise, either by free contribution or in the form of non-interest-bearing loans, will be matched by mixed Federal and State money as interest-free loans.

"A separate bill has been filed by the sponsors of this legislation which would make subscription charges deductible from taxable income.

"The bill further provides for a revolving construction loan fund of $10 million of Federal money. Without requiring any State participation, this sum will be loaned to cooperating prepayment plans for the special purpose of building and equipping small local medical centers for the group practice of medicine. This sum would provide for the setting up of about 125 new health centers at one time, with no burden on the States.

"By these means the establishment of a widespread, diverse system of voluntary plans will be fostered, including those that use group practice. In the long run those plans which supply the best and most extensive medical care for the subscribers will prevail. At every level there will be ample freedom for that creative initiative which alone can translate our American aspirations into reality."

Lest it be thought that S. 1970 relies solely on the development of government-aided voluntary plans to solve all the nation's health problems, reference to the summary of

the bill given at the beginning of this report will show that it includes provisions for direct aid for professional education, hospital construction and local public health units. Two additional features of the bill deserve special, if only brief, notice here.

Federal-State subsidies are provided to help bring adequate personnel and facilities to areas where acute shortages now exist. This is also found, though in less concrete form, in the Taft and Thomas bills, but S. 1970 adds a significant requirement. Such special aid may be granted only under a five year program formulated for an area by a District Health Council (which may cover an inter-State territory) that centers on a four year medical school and that provides for an integrated health service system of hospitals and professional personnel. Such programs will not come into being overnight but they are clearly essential if adequate health care is to be brought to many of the poor and sparsely settled regions of this country.

The other notable provision in the bill calls for a continuing, over-all but decentralized study of health needs and resources, and the formulation of 20 year local, State and national programs. The work would be under the supervision of a board similar to the "Hoover Commission on Reorganization of the Federal Government," but primary responsibility is placed on the Health Region Authorities and State Health Councils to study their own problems and to find their own solutions.

In so extensive a piece of legislation, there are bound to be many details on which those who are in sympathy with the general lines of the measure disagree. For example, the bill would exclude practicing physicians from the public policy boards at all levels, Federal, State and regional. The sponsors argue that providers of service should not be placed in the position of determining the basis of their remuneration under a public program; that if doctors are represented, hospitals, dentists, nurses and other health personnel would also have to be given a place. Advisory committees directly representing the professions are made mandatory for all the public bodies and these committees will have as much actual power as the public bodies themselves under other proposed measures —and, indeed, as is now the case under the Hill-Burton Act. Nonetheless, many physicians will undoubtedly feel that a minority of professional people should sit on every public board dealing with health problems.

Basically, S. 1970 fulfills to a large degree the requirements for a sound national approach to medical care as formulated in 1947 by the Committee on Medicine and the Changing Order of the New York Academy of Medicine. While it will require amendment in some particulars, it represents a genuinely native approach, based on years of serious investigation by both professional and lay people who are personally disinterested but dedicated to the advancement of American medicine. At the very least, S. 1970 deserves the serious study and earnest consideration of every physician.

TRENDS

IN HEALTH LEGISLATION AND ADMINISTRATION

By JOHN P. HUBBARD, M.D., *Contributing Editor*

This and subsequent descriptions of events and trends are intended to be unbiased and factual, presenting both sides of controversial matters so that conclusions may be formed from critical appraisal of things as they are. These statements do not necessarily reflect the opinion of the writer nor are they to be interpreted as official opinion of the Academy.

A MONTH ago we stated in this column that, in accordance with recently expressed policy of the Executive Board of the Academy, attention would be given henceforth to significant activities which are being directed toward the improvement of child health and which may, at least in part, have resulted from the Academy's Study of Child Health Services. We then reviewed the "Premature Infant Care Program" which has been instituted in North Carolina to meet deficiencies which had been revealed in the Study's "Pilot State."

While progress is being made along the front line of state programs, it is also gratifying to note progress in pediatric education.

Subsequent to publication of "Child Health Services and Pediatric Education," specific and detailed information for his own department was sent confidentially to each of the heads of pediatric departments of the medical schools. Thus, each department head could evaluate his own school in comparison with others. In reply we have received some rather dramatic evidence of the effective use which has been made of a knowledge of the facts. The following letter is only one of many of those received recently from deans and professors of pediatrics:

DEAR DR. HUBBARD:

Since Dr. John McK. Mitchell made his survey of the pediatric department of this medical school, a number of changes have taken place in which I thought you might be interested.

1. The Associate Dean, Dr. Knudson, has allotted for this year approximately 100 more hours in pediatrics. Beginning July 1, 1949, the Department of Pediatrics will have 312 hours as compared with 220 hours allotted to the department previously. As a result of this action, plans have been made for the complete reorientation of instruction in pediatrics.

2. As a result of this markedly increased allotment of hours, we have completely revised our teaching program for the second, third and fourth years. You will be interested to know that 178 of these hours will be strictly nondidactic work, namely: actual work on patients on the wards or in the outpatient department. The remaining hours are given over to the second year lectures, third year quiz conferences, fourth year ward rounds and third and fourth year amphitheater clinics. We have not, of course, included the overtime hours; but insofar as it is possible each fourth year pediatric student will be required to live in the hospital one week.

3. I realize that in the majority of schools the clinical clerkship is given in the third year. Our setup here does not provide sufficient clinical material in the outpatient to limit the fourth year work to such outpatient department.

4. Shortly after Dr. Mitchell's visit, Dr. Marjorie Murray began her work in teaching psychosomatic pediatrics. Instruction in this newer field of pediatrics will be partly lecture and partly clinical. The lectures will cover the following topics in the second and third years: psychologic aspects of child development, psychosomatic syndromes in childhood, nutritional and digestive disturbances, enuresis and toilet control, persistent infantile habits, tics, stammering, anxiety states and sleep disturbances, antisocial behavior and sex education. In addition the students will receive instruction, guidance and orientation in psychosomatic medicine in the outpatient clinics and on the wards. The purpose of the instruction will be to give the student some knowledge of the widespread existence of emotional problems in infants and children with and without somatic illness; orient him in the recognition of these emotional states; teach him the methods and attitudes employed by the physician in eliciting the causes of these emotional states and give him some insight into the methods of handling such conditions and some knowledge of their prevention.

5. We have plans underway which will materialize this fall to establish four additional pediatric clinics which will be used for teaching:

a. A model premature unit to be subsidized by the State Department of Health, to which prematures of the eastern half of New York State will be sent. One of our young pediatricians will be sent to New York this October to study with Dr. Levine in a brief brush-up course on prematures.

b. A child-health conference and clinic, subsidized by the State Department of Health and utilized for teaching physicians in 17 counties the method of running a modern child-health conference.

c. The establishment of a rheumatic disease clinic and research program. Dr. Gainor, one of our Board members, has completed the two weeks' course in rheumatic disease subsidized by the State Department of Health.

d. The hospital, with the cooperation of the departments of pediatrics, medicine and chest surgery, plans to open a congenital heart disease clinic.

6. Beginning July 1, 1949, the pediatric department has been granted a third assistant resident and a third intern. This will enable us to rotate these residents in a two months' rotation through St. Peter's Hospital, improving the quality of the work in that hospital and permitting us to assign fourth year students there for a portion of their ward work. The teaching will all be by members of the staff of the department of pediatrics.

7. Dr. Murray's teaching of psychosomatic pediatrics will be extended this year into the fourth year and will be strictly bedside teaching.

8. As of July 1, 1948, all babies born in this hospital are born on pediatrics. We at last have complete charge of all newborn infants with complete charge of the nurseries.

9. As of July 1, 1948, in cooperation with the State Department of Health, Division of Laboratories, we have offered BCG vaccination to all babies born in this hospital. This is to be a five year study of BCG vaccination in newborn infants.

I believe these improvements will go a long way toward correcting the glaring deficiencies of our previous teaching program, but will not provide an adequate budget so badly needed in attempting to run a modern department of pediatrics.

Sincerely yours,

(Signed) OTTO A. FAUST, M.D.
Professor of Pediatrics
Albany Medical College
Albany, N.Y.

INTERNATIONAL NEWS

NEWS FROM ENGLAND

ALAN MONCRIEFF, M.D., *Corresponding Editor*

DEPARTMENT OF CHILD HEALTH—MANCHESTER

Manchester is one of the latest of the British universities to establish a separate chair of child health. This title was chosen in preference to pediatrics to denote the increased interest being taken in the preventive aspects of medicine in general and of pediatrics in particular. It is also a term that is better recognized by the laity, to whom an appeal for funds to start the Department was made in 1944. As a result of this appeal annual donations were promised from Manchester and neighbouring local authorities and from the voluntary children's hospitals for a period of 5 years, and sufficient money was raised thereby to start the department in September 1947.

Prior to that date, there had been no special department, but the subject of diseases of children had been taught as part of the systematic course in medicine since 1913, and there was a reader in charge of the teaching and lecturing, together with a lecturer and 4 demonstrators—all part-time. The course in diseases of children lasted only 1 month and was limited entirely to the mornings.

The staff of the Department at present consists of a professor, a senior and a junior lecturer and a research worker, all full time, and a number of part-time demonstrators in clinical pediatrics together with a part-time clinical tutor. There is now a 3 months' course for every student and 1 month of this period is spent in residence. The other 2 months are divided between inpatient and outpatient work and during the latter period visits are arranged, in conjunction with the local authorities, to special institutions, residential nurseries, school clinics, child guidance clinics and the like.

Part of the period of residence is spent in the neonatal department of the maternity hospital; during this special period, teaching is given in the care of premature babies. There is an infant welfare clinic attached to the hospital and a pediatrician attends daily especially to give teaching in child health. A health visitor from the local authority service is seconded to this clinic and will take students with her on her domiciliary rounds during their period of residence.

Pediatrics is, from December 1949, to be recognized as a major subject in the final M.B., B.Ch., the qualifying examination of the University. There will be a separate paper and clinical examination with external examiners appointed.

One of the functions of the department is to train pediatricians to take charge of the outlying hospitals in the region, and the Manchester region is a large one with a population of more than 4 million people. Postgraduate work will, therefore, form an appreciable part of the teaching undertaken.

Manchester presents certain geographic drawbacks, for there are 2 children's hospitals, 2 general hospitals with large children's departments and an infants' hospital—and none of these is in the vicinity of the University and Medical School. The total number of beds for children is approximately a thousand, but because of their dispersal only 250 can be utilized for teaching purposes. The main children's hospital, the Royal Manchester Children's Hospital, is some 4 miles out. Thus, transport difficulties have to be overcome, but until the projected Institute of Child Health is built they will continue. An "island site" has been planned for the development of the University and on this site all medical facilities will be provided, including a new Institute of Child Health comprising the department and a children's hospital of about 200 beds. It is not anticipated that this development will be completed before 1960.

Co-operation with the health services is effected by lectures, clinics and consultations. Clinics are interchanged when opportunity offers. Lectures are given by members of the department to school medical officers, infant welfare officers, health visitors and midwives. There is a weekly cardio-rheumatic clinic run in conjunction with the Education Department.

It is hoped to have in the near future more active co-operation by means of reciprocal appointments, the school medical and infant welfare medical officers coming in to the hospital for clinical work, and during such periods the Department of Child Health providing medical officers to do

school inspections and welfare clinics. Lack of staff in the Department is the chief drawback to the spreading of this excellent system. There are 10 or more local authorities in the region with a medical staff of something like 50, so the necessary reciprocity staff in the Department may be imagined.

Refresher courses for general practitioners are held at intervals and practitioners are also invited to attend the monthly clinical conferences at the Children's Hospital.

A pediatric club was launched last year in Manchester, to promote further co-operation between pediatricians and child health workers and, in addition to scientific papers read by the members, distinguished visiting pediatricians have given lectures. These include Professor Kerpel-Fronius, Dr. Dorothy Andersen, and Professor Lichtenstein.

Research work at present is confined to the clinical sphere because of lack of facilities. An anthropometric survey of a cross-section of school children is being undertaken in conjunction with the Department of Dentistry; bacteriologic research is conducted by a fellow working in the Department of Bacteriology, and cardiologic investigations are similarly linked with the Department of Cardiology at the Manchester Royal Infirmary, the main university teaching center in clinical medicine.

The administrative offices of the Department are at present housed in the Maternity Hospital which, in the absence of a recognized university teaching hospital in pediatrics (the Royal Manchester Children's Hospital is not in the "teaching group" of hospitals yet, but it is hoped that in the near future it may be so designated) is the next best place for them, and collaboration with the obstetric department is of the closest, in every sense.

WILFRID GAISFORD, M.D., F.R.C.P.

NEWS AND ANNOUNCEMENTS

American Pediatric Society

At the Annual Meeting of the American Pediatric Society, held on May 4, 1949, in the Marlborough-Blenheim Hotel, Atlantic City, N.J., the following members were elected officers of the Society for the year 1949-1950:

President—Philip C. Jeans, Iowa City
Vice President—Katharine Dodd, Cincinnati
Secretary-Treasurer—Henry G. Poncher, Chicago
Recorder and Editor—Stewart H. Clifford, Boston

Because of Dr. Dunham's resignation from the Council and Dr. Lyttle's decease, in addition to the regular new members, three members were appointed to the Council this year: George M. Guest, Cincinnati; William L. Bradford, Rochester, N.Y.; Harry H. Gordon, Denver.

The following candidates were elected to Active Membership in the Society: Aims C. McGuinnes, Philadelphia; Gladys J. Fashena, Dallas; Alton Goldbloom, Montreal; John McK. Mitchell, Philadelphia; Antonio M. Ortiz, Santruce, Puerto Rico; Paul V. Wooley, Detroit; Wolf W. Zuelzer, Detroit; Henry L. Barnett, New York, and Edward C. Curnen, Jr., New Haven.

The next annual meeting will be held at French Lick Springs, Indiana, in May 1950.

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The Children Show, an exposition devoted exclusively to products and services for children will be held in Los Angeles, just preceding school opening, Sept. 10 through 18, 1949, at Los Angeles' Shrine Convention Hall. It is being sponsored by the Society for the Advancement of Health and Education, a nonprofit corporation. It will include exhibits, educational and entertainment features.

Show exhibits will include clothing, sporting goods, schools, camps, playgrounds, pets and supplies, toys and games, photographers, prenatal guidance, insurance, furniture, medical and dental products and services and others. Special features will be lectures, panel discussions, a parents' clinic, motion pictures, radio and television broadcasts, daily birthday parties, entertainment, child talent contests, prizes and a children's amusement area and nursery.

Advisory organizations are the Parent Teachers Association, the Chamber of Commerce, the Los Angeles Department of Health, Los Angeles City Schools and others.

* * *

The July issue of UNICEF NEWS, vol. 1, no. 6, 1949, is given in large part to the story of Calmette, co-discoverer of BCG, the vaccine against tuberculosis that is now being used to protect children throughout the world. His story, in relation to the work now being carried forward with the help of the Children's Fund, is told here for the first time. Copies and photographs are available from: United Nations International Children's Emergency Fund, 405 E. 42nd St., New York City.

* * *

Fellows of the American Academy of Pediatrics are cordially invited to join the Special Train Party for the Annual Meeting in November, from Chicago to the convention city, San Francisco. An attractive booklet descriptive of this tour may be had by addressing Mr. W. M. Maloney, Passenger Agent, Room 711, 105 W. Adams St., Chicago 3, Ill.

* * *

The election of Dr. Rustin McIntosh as president of the medical board of the Presbyterian Hospital in the City of New York was announced recently by the hospital's president, Charles P. Cooper. Dr. McIntosh replaces Dr. George F. Cahill, who has served three years as president.

* * *

Dr. Lee E. Farr has been appointed head of the Medical Department at Brookhaven National Laboratory, Upton, Long Island, N.Y.

* * *

Dr. Horace L. Hodes, formerly of Baltimore, has been appointed Director of Pediatric Research at Mt. Sinai Hospital, New York City.

BOOK REVIEWS

THE NORMAL CHILD, Alan Brown, M.D., and Elizabeth Chant Robertson, M.D., Ph.D., ed. 4, Toronto, McClelland & Stewart Limited, 1948, $3.00, 258 pp.

This 4th edition has been entirely rewritten with the assistance of Dr. Robertson, who is also at the Toronto Hospital for Sick Children. It is primarily for the guidance of parents and has chapters on such topics as prenatal care, breast feeding, diet, development, illness and accidents. It is carefully, clearly written and up-to-date. There is a lot of practical material, such as lists of play things and suggestions for summer vacations. The recommendations for feeding schedules and diet are conservative compared to usual American customs.

Psychologic advice in such matters as thumb sucking, toilet training and discipline follows the present day tendency to stress understanding and the avoidance of unnecessary interference. However, unsupported arbitrariness crops out, and the explanations given for children's motives rely too often on superficial concepts, such as the over-worked "desire for attention."

Much of the book is reassuring in tone. But there are also passages that seem needlessly alarming. "If your runabout baby chews lead containing paint—he will likely develop lead poisoning which causes convulsions also. Blindness, mental deficiency or even death may be the end result of eating lead. . . ." In a discussion of the advantages of breast feeding a research study is referred to as follows: "Only 7% of the deaths that occurred were in breast fed infants but 66% of the babies that died were bottle fed!" Many who have studied the emotional disturbances of present day western mothers and children feel that one of the serious causes is the unnecessary anxiety created by well meaning physicians and health educators. It should be possible to give health advice that will have maximum efficacy without arousing disproportionate panic, especially in that conscientious portion of the population which consults physicians and child care books.

CARDIAC CATHETERIZATION IN CONGENITAL HEART DISEASE, Andre Cournand, M.D., Janet S. Baldwin, M.D., and Aaron Himmelstein, M.D., New York, The Commonwealth Fund, 1949, $4.00, 116 pp.

Among the newer methods of diagnosis in congenital malformatons of the heart, cardiac catheterization holds an important place. The authors set forth the essentials of this diagnostic approach.

The monograph is divided into 2 parts. The 1st part deals with the equipment, technics and procedures involved, the roentgenographic observations, the patterns of the blood pressure tracings and the methods of computation of systemic and pulmonary blood flow. The importance of a well trained team to carry out these studies with accuracy and safety is emphasized.

The 2nd portion of the book comprises 17 illustrative cases of congenital malformations of the heart in which the clinical data and the findings obtained by catheterization are coordinated and the diagnostic possibilities discussed.

The work is well presented and can be highly recommended not only to physicians who plan to undertake this very specialized procedure but also to those who wish to familiarize themselves with this diagnostic method.

BACTERIAL AND MYCOTIC INFECTIONS OF MAN, Rene J. Dubos, Ph.D., Philadelphia, J. B. Lippincott Company, 1948, $10.00, 784 pp.

This book is designed to present for the medical student and practicing physician the present state of knowledge concerning bacteria, actinomycetes and molds which cause disease in man, together with discussions of host-parasite relationships, epidemiology, immunology, chemotherapy and related subjects. A companion volume, "Virus and Rickettsial Diseases of Man," is published separately and the 2 volumes retail for $10.00. Thirty-four experts in various fields contribute the 37 chapters. There are 784 pages on semi-gloss paper, the print size is adequate, no typographic errors were noted and the book is well illustrated and a convenient size for student use.

The arrangement of subject material is similar to previous textbooks of bacteriology, the first 200 pages being devoted to chapters on the history of medical bacteriology, morphology and

physiology, host-parasite relationships, allergy, immunology and blood groups. Then follows a chapter on each of the pathogenic bacteria, the actinomycetes and medical mycology. The last section of the book is devoted to normal flora of the mucous membranes, sterilization, chemotherapy, epidemiology and an excellent chapter on cultivation and identification of pathogenic bacteria. A remarkable uniformity of presentation and style reflects painstaking editorial effort. Each subject is authoritatively presented and interpreted by a specialist and the tremendous recent advances in many fields are stressed. The simplicity of presentation without numerous references makes for clarity. The book should be well received by students, practitioners and research workers as a concise, authoritative and up-to-date source of information. However, the lack of comprehensive references will detract from its usefulness as a reference book. The chapter on bacteriology of mucous membranes might well be modified to include discussion of the normal flora of the skin and perhaps of the tonsillar fossa and nasopharynx since in clinical practice these areas are cultured more frequently than any other.

THE CHILD IN HEALTH AND DISEASE, Clifford G. Grulee, M.D., and R. Cannon Eley, M.D., Baltimore, Williams & Wilkins Company, 1948, $12.00, 1006 pp.

"The Child in Health and Disease" is based on the thesis expressed in the preface—". . . to correct the emphasis on investigation (which) has led to . . . . a feeling of complacency when the practical side of pediatrics has come to the fore. We are prone to forget that the value of medical investigations depends upon its practicable application as the final test of its usefulness." This ambition is most commendable, since the science of medicine has made such tremendous strides during the past 2 decades. This more spectacular picture tends to warp the attitude of both the teacher and the student.

Sections I, II and III deserve special commendation in carrying out the above thesis. In these sections, growth, development, physiology, feeding, nutrition and pathology are clearly and adequately discussed for a text of this size. There creeps into various authors' manuscripts, however, certain dogmatic statements which can be challenged, i.e., "Vitamin K should be administered immediately after birth." Such statements are not good for medical students or physicians not familiar with the unpredictable behavior of the newborn infant or in expressing the concept of the volume.

Sections V to XIX which discuss "Acute Infections," "Chronic Infections," various "Tracts" or systems and "Miscellaneous Subjects" are clear and adequately covered. Generally, each author has emphasized etiology, symptomatology and diagnosis. Chemo- and antibiotic therapy are as up-to-date as rapid progress in these fields warrants. It is unfortunate that 1 or more authors expressed their individual opinions without due deference to opinions of colleagues in their own special field. This is not to be condoned in a text.

The arrangement of subject matter for quick reference is good. The index and contents are quite adequate. While the general format and double column printing makes for easy reading, small type for paper conservation is deplored. A number of minor typographic errors were found. The cuts and charts are clear and illustrative of the subject at hand.

"The Child in Health and Disease" is a worth while addition to a pediatric library despite criticisms which the reviewer thinks justifiable.